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USSR Space Life Sciences Digest

Issue 20

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USSR Space Life Sciences Digest: Issue 20 Reader Feedback Form

To our readers: We are working in a large number of highly technical, specialized areas for which adequate Russian-English glossaries have yet to be compiled. We ask your help in improving the accuracy and specificity of our English terminology. Please fill out the form below whenever you encounter an incomprehensible, incongruous, awkward or otherwise inappropriate term. While we solicit all suggestions for improved renderings, the statement that a term is inappropriate provides us with useful information, even when no better alternative can be suggested. A copy of this form will appear in all future issues of the Digest. Thank you for your help.

Abstract #	Incorrect or contextually inappropriate word or phrase:	Suggested rendering: ("??" is an acceptable entry)
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FROM THE EDITORS

This is Issue 20 of the USSR Space Life Sciences Digest. We would like to thank the approximately 200 individuals who responded to our third reader survey. We were most gratified to have 100 people volunteer to provide us with occasional help concerning technical terminology. A list of volunteers organized by field of expertise is being compiled and some of you may be hearing from us shortly. Of course, we always welcome unsolicited suggestions concerning terminology (See form on preceding page.) The primary alteration in this issue based on survey responses is a more detailed emphasis on exact procedures used in experiments. However, readers should recognize that the kind of explicit description of procedure typical of Western scientific papers may be absent in Soviet ones. Almost as many people requested fuller information on statistics as on procedures. We will make it a policy to provide all available information on statistical tools used to analyze data; however, again this information may not be provided in the original Soviet article. By far the most common statistic used by the Soviet researchers we abstract is Student's t , known also as the t -test or t -ratio. This test is commonly used for multiple comparisons within a single experiment.

This is the last issue of the USSR Space Life Sciences Digest to be produced on our old computer system; our new system should provide us with better tools to improve Digest appearance and format and to follow additional suggestions made by our readers. An index of Digest issues 15-20 is being compiled and should be distributed shortly after the present issue.

Abstracts in the present issue presenting or discussing space flight data are: Body Fluids CR11; Cardiovascular and Respiratory System P916; Metabolism P922; Musculoskeletal System P915, P923, P935, P944, M137; Neurophysiology P936, P939, P940; Reproductive Biology P937, P938.

We would like to express our appreciation for the valuable help provided by Dr. Gary Coulter of NASA and Dale Andersen of Lockheed in the preparation of this issue.

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ADAPTATION

(See also: Musculoskeletal System P944, M137; Operational Medicine P911)

MONOGRAPH:

M141(20/88) Platonov VN.

Adaptsiya v sporte [**Adaptation in Sports**].

Kiev: Zdorov'ya; 1988.

[216 pages; 25 tables; 116 figures; 279 references; 101 in English]

KEY WORDS: Adaptation, Musculoskeletal System, Athletes, Individual Differences, Exercise, Sports, Fatigue, Energy, Human Performance

Annotation: This monograph considers the adaptive restructuring that occurs in physiological systems of athletes who are training for competition. The author focuses on individual differences in adaptive restructuring and the different responses in each physiological system. This book is intended for scientists, trainers, and athletes.

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BIOLOGICAL RHYTHMS

(See also: Cardiovascular and Respiratory System P912)

MONOGRAPH:

M142(20/88) Gudkova SYa.

Mekhanizmy zimney spyachki [**The mechanisms of hibernation.**]

Pushchino: USSR Academy of Sciences; 1987.

[206 pages]

Affiliation: Scientific Center for Biological Research; Institute of Biophysics

KEY WORDS: Biological Rhythms, Hibernation, Sleep, Metabolism, Cold, Neurophysiology, Body Fluids, Endocrinology, Enzymology, Hematology, Gastrointestinal System

Annotation: This collection includes the results of research performed during the last 2 years in the area of hibernation and sleep-like states (dormancy, torpidity?). Particular emphasis is placed upon biophysical and biochemical research on peripheral regulatory mechanisms governing hypometabolic natural states on the cellular, subcellular, and molecular levels. The collection contains the most current data on the "trigger" mechanisms of torpor, description of an evolutionary approach to the understanding of natural hypometabolic states, discussion of the characteristics of structural homeostasis and the kinetics of proliferation. This work will be of interest to a wide ranges of biophysicists, biochemists, physiologists, and clinicians.

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BODY FLUIDS

(See also: Biological Rhythms M142)

PAPER:

P932(20/88)* Zhidkov VV, Lobachik VI, Borisov GI, Zaychik VYe, Fedorov YuV, Biryukov YeG.

A micromethod for measuring volume of extracellular fluid.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 86-89; 1988.

[15 references; 3 in English]

Body Fluids, Extracellular Fluid

Humans

Equipment and Instrumentation, Micromethod

Abstract: In this paper, the authors describe a method they have developed to overcome the shortcomings of existing procedures for studying extracellular fluid volume. This method measures extracellular fluid volume by administering diluted stable bromine and measuring its concentration in whole blood using X-ray fluorescent analysis. Subjects ingest 10 ml of 10% sodium bromide in water. In 6 to 12 hours, two blood samples of 10-50 μ l are taken from the finger. One sample is used to determine hematocrit through centrifugation, and the other is placed on a substrate of decalcified filter paper with surface density of 7 mg/cm², which has been treated with cleol. The sample is surrounded by a liquid paraffin ring. Five test samples are prepared from each blood sample and results are averaged. The test sample is dried to a constant mass in 2 hours at room temperature. Bromide concentration and measurement error are measured using an automated X-ray fluorescent analyzer consisting of an automated carousel for replacing samples, a measurement head with a system of diaphragms, an X-ray source with maximal voltage on the tube of 45 kV and current of 1 μ A, a detector with energy resolution of 185 eV on a line 5.9 keV with a primary amplifier, and a multichannel analyzer with a microprocessor. The spectrum of characteristic bromide radiation with energy of 11.9 keV is recorded and processed on the multichannel amplitude impulse analyzer with a microprocessor. The spectrum is measured for 30 seconds. Calibration standards were developed by adding a known quantity of water solution of bromine to whole blood. Extracellular fluid volume was determined with the formula:

$$ECV = 0.86 \frac{Q \cdot (100 - Ht) / 100}{C_t - C_0},$$

where Ht is hematocrit (in percent), Q is quantity of bromine introduced (in mg), C_0 is the initial concentration of bromine in blood (in mg/ml), and C_t is concentration of bromine in blood after equilibration; 0.86 is Olesen's coefficient, which accounts for the concentrations of proteins in blood, and also bromine in erythrocytes and epithelial cells in the the intestine. This method was compared to the most commonly used method, which utilizes the radionuclide Na⁸²Br as an indicator.

BODY FLUIDS

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The newly developed method was concluded to have the following advantages:

- the amount of bromine that must be introduced in the body is one tenth of that required by the traditional method, decreasing the time required to perform repeated measurements in an individual;
- the new method takes blood from the finger rather than puncturing a vein, reducing trauma;
- the amount of blood required for analysis is reduced by a factor of 200 - 1000;
- the difficulty of the procedure is reduced considerably for the experimenter;
- since the blood can be kept in its dried form for a longer period of time, the test is more suitable for space flight;
- error is reduced to $\pm 3.2\%$.

CONFERENCE REPORT:

CR11(20/88) Ivanovna LN.

Report on: Conference on **Problems of Physiology and Pathology of Calcium Metabolism and Its Regulation**, Riga, November, 1987.

Fiziologicheskiy Zhurnal.

LXXIV(6): 903-905.

KEY WORDS: Body Fluids, Renal Physiology, Metabolism, Fluid-Electrolyte Metabolism, Calcium, Nutrition, Vitamin D, Vitamin K, Space Flight, Hypokinesia, Exercise

In accordance with the agenda of the Ad Hoc Commission on Renal Physiology and Fluid-Electrolyte Metabolism, the Scientific Council on the Physiology of Visceral Systems of the USSR Academy of Sciences convened a conference devoted to problems in the physiology and pathology of calcium metabolism and its regulation. This conference was held from 24 to 26 November in Yurman at the facilities of the Riga Medical Institute. The major goal of the conference was discussion of the current status of this extremely important area of basic and applied research. Approximately 30 scientists from various institutions in Moscow, Leningrad, Riga, Novosibirsk, Donetsk, and Tblisi participated.

Papers concerning the theoretical aspects of the problem discussed the biological role and regulation of calcium metabolism in human beings and animals. V.K. Bauman considered current concepts of the mechanism underlying absorption of calcium in the intestine and evaluated the different views of the structure and functioning of the system responsible for calcium transport across the intestinal epithelium. He stressed that many of the issues in this area are still unresolved. Yu.V. Natochin described in detail the mechanisms underlying calcium transport in the nephron and emphasized that the roles played by neural and hormonal factors and other biologically active substances in regulating reabsorption of this ion are still unresolved. He discussed results implying that calcium can regulate the activity of sodium channels in the apical membrane of epithelial cells. Calcium regulation of water permeability in this membrane evoked great interest. S.N. Orlov described experimental results on the mechanisms of calcium transport across cell membranes and the relationships among the calcium-accumulating activity of the membrane fractions of various tissue types. G.N. Baldenkov presented interesting new data concerning the role of calcium in mediating the action of physiologically active substances and peptide hormones. L.N. Ivanovna demonstrated that, although the modulating effect of calcium can be observed at various stages in the intracellular chain of events induced by a hormone, the mechanism underlying this effect remains unclear in many instances. I.P. Yermakova presented an analysis of parameters that measure calcium in blood and its association with protein and low molecular weight components of plasma in the norm and under pathological conditions. A.M. Gerasimov examined the interaction of calcium metabolism and peroxidation from an evolutionary perspective. V.B. Spirichev discussed the effect of alimentary factors on calcium homeostasis and assigned an important role to the vitamin D hormonal system in the regulation of calcium metabolism. I.N. Sergeyev provided new data concerning the role of vitamin K in calcium metabolism.

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The participants devoted considerable attention to the pharmacological aspects of regulating calcium metabolism. G.Ya Dubur presented new data concerning the mechanism underlying the effects of calcium antagonists, discussed the characteristics of three recently synthesized antagonists, and demonstrated the potentiating influence of calcium antagonists on the cytostatic effect. Material relevant to the association between the chemical structure and biological activity of analogues and metabolites of vitamin D was analyzed in detail. N.A. Bogoslovskiy described the properties of a new analogue -- oxidevit, synthesized by the "Vitamin" Scientific-Manufacturing Association, which has a powerful therapeutic effect. E.A. Yur'yev discussed correction of calcium metabolism pathology using diphosphates and K.A. Merzon spoke on the criteria used by clinicians to evaluate calcium metabolism.

Another group of papers covered the pathophysiological and clinical aspects of calcium metabolism. V.S. Akmatov considered data on the state of the bone system and hormonal balance in cosmonauts on flights varying in duration and in volunteer subjects undergoing long-term hypokinesia with head-down tilt. He discussed prevention of negative calcium balance and the significance of pharmacological correction and physical exercise in preventing bone demineralization. The need to determine the extent of demineralization under various flight conditions and special regimens was noted. It was agreed that the new methods of evaluating bone density developed in the Institute of Biomedical Problems of the USSR Ministry of Health should be introduced into clinical practice. S.M. Kotova discussed the diagnosis and treatment of calcium metabolism pathology which leads to osteomalacia and results from decreased calcium absorption in the intestine with accompanying enteropathies and bile secretion disorders. L.Ya. Rozhinskaya extended this discussion to disorders of calcium metabolism caused by hormonal imbalance, particularly those associated with intensive treatment with glucocorticoid. Special mention was made of the positive effect of oxidevit treatment for this sort of pathology and stress was placed on the need to develop detailed differential diagnostic criteria for designing treatment strategies. V.K. Leont'yev discussed stomatological problems and noted that many questions relevant to the pathogenesis of stomatological disease in disorders of the mineral composition and pH of saliva, and their treatment with various mineral compounds, have not yet been resolved. I. M. Lanskaya argued that one of the most urgent problems in nephrology is the disruption of calcium homeostasis associated with prolonged or regular hemodialysis. Discussion of this and related issues produced agreement that further attention was required to individually tailor the mineral composition of the dialysis solution is essential. N.A. Reynser discussed the differential diagnosis and treatment of hypercalciuria due to diet or to rate of absorption of calcium and phosphates, etc. Particular stress was placed on the need to develop common tests for evaluating parameters of calcium homeostasis, the lack of which makes it difficult to compare the results obtained in different laboratories and clinics.

In the final paper, D.A. Babarykin discussed the potential for correcting disorders of phosphorus and calcium metabolism associated with various pathological states and clearly posed the most pressing problems (mechanisms of calcium transport in specialized tissues, interaction of vitamin D

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metabolites and synthesized analogues in the regulation of calcium metabolism, characteristics of intracellular regulation of vitamin D₃, indicators and contraindicators for combined hormone-vitamin D therapy in different types of calcium pathology).

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

PAPERS:

P912(20/88) Galichiy VA.

Characteristics of biological rhythms in external respiration parameters in humans during tilt tests.

Fiziologiya Cheloveka.

14(4): 577-585; 1988.

[14 references; 3 in English]

Cardiovascular and Respiratory Systems, External Respiration; Biological Rhythms

Humans

Tilt Tests

Abstract: The goal of this work was to perform biorhythm analysis of a number of respiratory parameters in humans undergoing tilt tests in which they were placed in passive upright position. A total of 5 healthy males, aged 26 to 40, participated. A passive tilt test placing them in upright position was performed in the morning before breakfast. External respiration was assessed by measuring parameters of respiratory minute volume (V_E), minute volume of absorbed oxygen (V_{O_2}) and exhaled carbon dioxide (V_{CO_2}), respiratory coefficient (R), partial oxygen and carbon dioxide pressure in alveolar air (pA_{O_2} and pA_{CO_2}), and oxygen utilization coefficient (O_2UC). Before the tilt test, the subjects spent 10-13 minutes on the tilt table in a horizontal position, during which baseline parameters were recorded for a 10-minute period. Immediately afterward they were placed in a vertical (head-up) position with the body at a 70° angle to the horizontal. The aforementioned parameters were recorded throughout the 20-minute period that subjects remained in this position. Parameters were measured using a metabolimeter and gas analyzer. During the first 8 minutes of the baseline period, parameters were averaged every 2 minutes and in the subsequent period (including the tilt test period) every 30 seconds. With the exception of the oxygen utilization coefficient, all parameters were expressed as a percentage of the mean baseline value. Thus, a series of 40 values was obtained for every parameter, each value representing data accumulated over a 30-second period. Since data fluctuated over the course of the measurements, amplitude and frequency characteristics of these fluctuations were analyzed. The period of each fluctuation was defined as the distance between two adjacent minima, while the amplitude was the difference between the maximum and minimum of each cycle. Maxima, minima, and amplitudes were all expressed as percentages, allowing the fluctuation amplitudes of various parameters to be compared. At various stages during the tilt test, correlations among a number of the parameters were evaluated and tested for statistical significance. The derived parameter of alveolar ventilation $\dot{V}_A = \frac{\dot{V}_{CO_2} \cdot 100}{F_{ACO_2}}$ was also used in this analysis.

Throughout the tilt test, the parameters fluctuated in a cycle with a period of about 1 minute. There was great similarity in amplitude and period between V_{O_2} and V_{CO_2} ; and amplitudes of fluctuation of pA_{CO_2} and pA_{O_2} . Both increases and decreases with respect to baseline were noted in different mean parameters values during tilt test. pA_{O_2} only increased, pA_{CO_2} only decreased, and other parameters underwent changes in both directions at

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different times during the period. The most interesting effects occurred in the initial period of the tilt test. The parameters \dot{V}_{O_2} and \dot{O}_{2UC} entered a negative phase (i.e., were below baseline) during the first minute after the shift in position, reaching a minimum value (19-22% decrease) in minutes 2-3 and continuing to be depressed until minute 4-6 of the test. \dot{V}_E and \dot{V}_{CO_2} dropped below baseline only after 2.5 minutes and the decrease was shorter and less extreme than in the previous case. The respiratory coefficient was above baseline in the first minute after assumption of the vertical position and this positive phase lasted 5 minutes with the maximum being 22% above baseline. Correlation between \dot{V}_E and \dot{V}_{O_2} was high positive for all 2-minute periods during the tilt test except during minute 4 - 7, when there was no correlation. Correlation between \dot{V}_E and \dot{V}_{CO_2} was high and positive, with the exception of minutes 4 - 7 when it was low and negative.

Correlation between \dot{V}_A and \dot{V}_{O_2} was high and positive for minutes 1-3 and 7-13, moderate and positive in minutes 14-20, and high and negative for minutes 3-7. Correlation between \dot{V}_A and \dot{V}_{CO_2} was high and positive for minutes 1-13; and moderate and positive during minutes 14-20. Thus the first 7 minutes of a tilt test are marked by decreased oxygen utilization and disruption of coordination among the various components of the pulmonary ventilation system. These effects are related to the difficulties associated with adaptation to an upright position. Functions begin to stabilize only by minute 13-14.

The authors come to the following conclusions:

1. In passive upright position, the external respiration parameters studied undergo cyclic fluctuations with periods of about 1 minute.
2. The period between minutes 4 and 7 of a tilt test is marked by lack of coordination among the individual components of pulmonary ventilation, possibly due to stress and difficulty associated with adaptation to the upright position.
3. When studying the cardiorespiratory system in a tilt test, it is desirable to focus on the depth and duration of the negative phase of the parameters of \dot{V}_{O_2} and \dot{O}_{2UC} , because there is reason to believe that the severity of this phase is an indirect indicator of the effectiveness of compensation for hemodynamic shifts caused by a shift to vertical position.

Table 1: Period and amplitude of fluctuations in parameters of external respiration during a 20-minute tilt test

Table 2: Values of the coefficients of correlation of \dot{V}_E and \dot{V}_{O_2} and \dot{V}_{CO_2} at various periods during a tilt test

Table 3: Values of the coefficients of correlation of \dot{V}_A and \dot{V}_{O_2} and \dot{V}_{CO_2} at various periods during a tilt test

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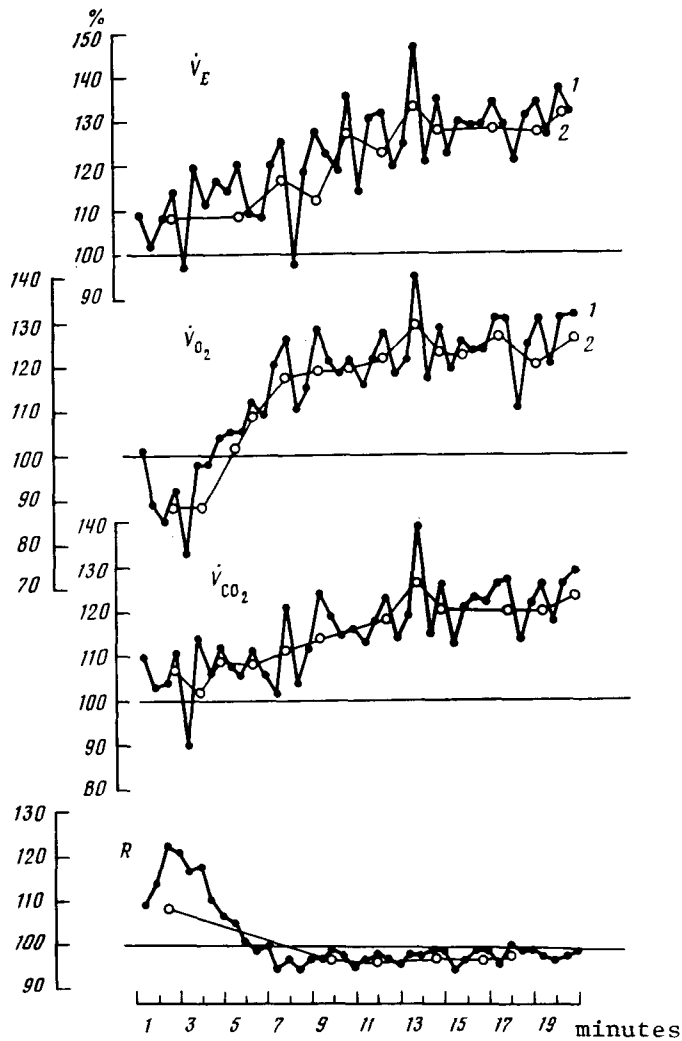


Figure 1: Changes in parameters of external respiration (1) and changes in their level (2) during a tilt test

\dot{V}_E - respiratory minute volume; \dot{V}_{O_2} - minute volume of absorbed oxygen;
 \dot{V}_{CO_2} - minute volume of exhaled carbon dioxide; R - respiratory coefficient.
 Abscissa -- duration of tilt test; Ordinate - % of baseline value.

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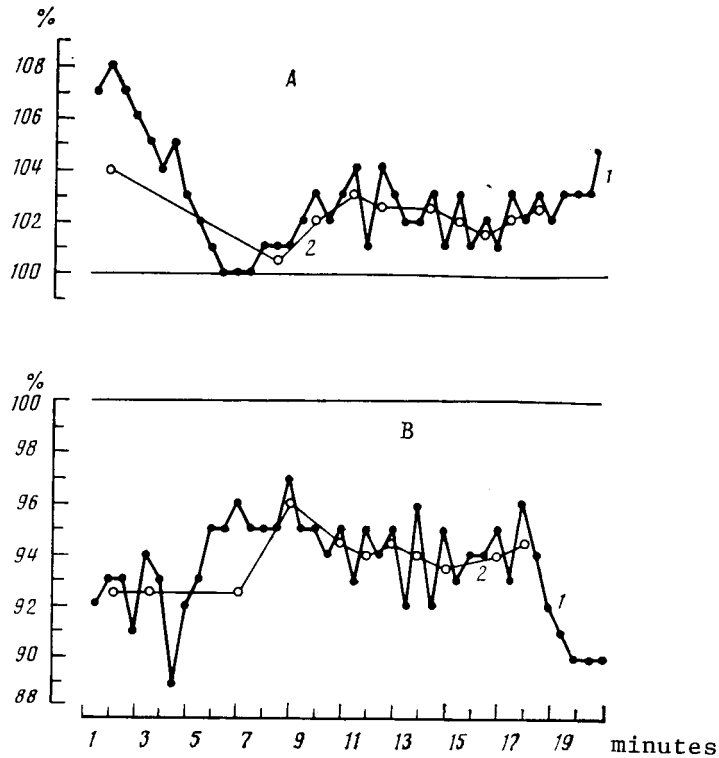


Figure 2: Changes in parameters of partial pressure of oxygen (A) and carbon dioxide (B) in alveolar gas (1) and changes in their levels (2) during a tilt test

Key: as in Figure 1.

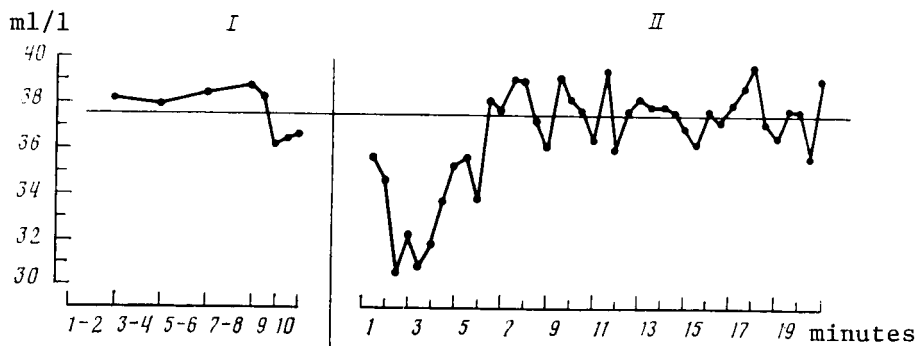


Figure 3: Mean group curves of dynamics of oxygen utilization coefficients in horizontal position (I) and after tilt to vertical (II)

Abscissa: time; Ordinate - O₂UC, ml/l

Figure 4: Individual curves of O₂UC in horizontal position and after tilt to vertical

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

P916(20/88)* Yegorov AD, Alferova IV, Polyakova AP.

State of cardiodynamics under conditions of long-term weightlessness.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 19-26; 1988.

[26 references; 10 in English]

Cardiovascular and Respiratory Systems, Cardiac Cycle

Humans, Cosmonauts

Space Flight, Salyut-6, Salyut-7, Long-Term; LBNP, Physical Exercise

Abstract: This paper summarizes and draws conclusions about cardiac dynamics based on analysis of phase cycle dynamics in 17 cosmonauts during flights lasting 96-237 days on board the Salyut-6-Soyuz and Salyut-7-Soyuz space station complexes. Cardiac cycle dynamics were measured kinetocardiographically from the region of the apex beat of the heart using an onboard apparatus. An EKG, using DS leads, was also recorded. The following parameters were measured: duration of cardiac cycle, mechanical systole, diastole, ejection period, filling period, isometric contraction and isometric relaxation phases, rapid filling, slow filling and auricle contraction. Derived parameters included initial rate of increase of intraventricular pressure ($V_i = BP_{dis} - 5$)/isometric contraction, mm Hg) and mean rate of ejection of blood from the left ventricle (ratio of stroke volume to ejection period, ml/sec). Phase structure of the cardiac cycle was measured under conditions of relative rest and in functional tests involving lower body negative pressure (LBNP) and graded physical exercise. LBNP was applied using a pneumovacuum suit which was hermetically sealed at the level of the crest of the iliac bones. The decompression schedule was 125 mm Hg for 2 minutes, -35 mm Hg for 3 minutes. An exercise test was conducted on a bicycle ergometer with mean work of 750-800 kGm/min for 5 minutes. Data analysis included a two-factor analysis of variance and the S-method of multiple comparisons, which enabled study of the effects of long-duration flight, comparison of mean values, and identification of periods in which parameters differed reliably from preflight values.

Results for cosmonauts at rest are presented in Table 1. Duration of cardiac cycle and associated parameters of mechanical systole, diastole, ejection period, and filling period increased insignificantly during month 1 of flight and in subsequent months decreased or returned to normal. The phases that are not closely associated with cardiac cycle duration underwent statistically significant changes. The isometric contraction phase decreased by a maximum of 10% and isometric relaxation by 33-34%, while the rapid filling phase increased by 27-31%. These changes reflect a functional restructuring of cardiac activity, which is conceptualized in Diagram 1. This restructuring develops primarily during month 1 of flight; months 2-8 are marked by relative stabilization with cardiac phase structure parameters tending to normalize.

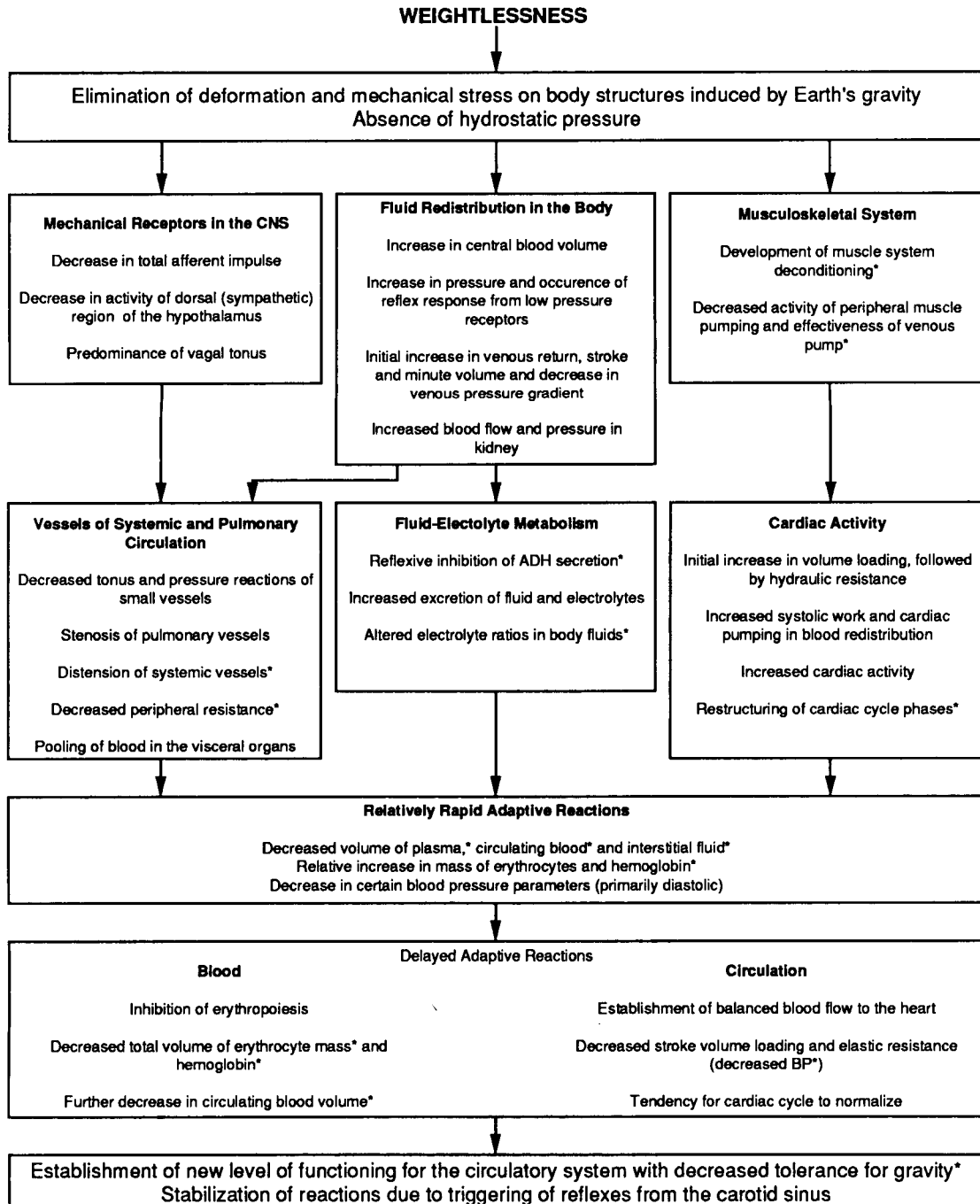
Tests with LBNP produced changes in cardiac parameters (compared to pretest levels) similar in direction to those occurring preflight. In both cases, duration of the cycle, mechanical systole, diastole, filling period, and slow filling all decreased, while isometric contraction and relaxation phases increased in duration. However, there were a number of differences: isometric contraction increased to a greater extent in space, V_i decreased in space in response to LBNP but remained the same on Earth; rapid filling increased in response to LBNP preflight but decreased in space. Changes in

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

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Diagram 1

General schematic model of the mechanisms underlying changes in the cardiovascular system in response to weightlessness



* Space flight data

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total duration and in mechanical systole and auricle systole were more marked in space during month 1 only, while response of the isometric relaxation phase grew more pronounced during the later portion of the flight. Both before and during the flight, the LBNP test evoked signs of decreased volume loading on the heart and decreased contractile force suggesting the development of myocardial hypodynamia syndrome. Changes occurring in the cardiac cycle in response to LBNP were different (in extent not direction) in month 1 and months 2-8, as can be seen in Figure 1. These differences imply that underloading?? of the heart in response to LBNP is more severe during months 2-6 of flight.

A graded physical exercise provocative test was conducted to assess compensatory-accommodative mechanisms and status of the cardiovascular system, as well as the physical work capacity of the cosmonauts. In pre- and inflight tests, cardiovascular parameters were measured during the first minute after exercising and compared to pretest values. Both before and during the flight, exercise led to a marked postexercise shortening of total cycle duration, mechanical systole, ejection period, diastole, filling period, slow filling phase, and auricular systole. Both isometric contraction and relaxation phases were shortened. The only difference between pre- and inflight response was that the rapid filling phase decreased in duration in flight and increased preflight. Mechanisms underlying the effects of provocative tests inflight are presented in Diagram 2. The authors emphasize that extensive countermeasures were used by the cosmonauts who were subjects for this study. The authors conclude that the changes in cardiac cycle occurring in space, both at rest and in response to provocative tests, do not progress during long-term flights and may be considered adaptive responses to weightlessness.

Table: Changes in mean values of major parameters of cardiac activity in cosmonauts at rest during long-term space flights

Parameter	Preflight	Flight	
		Month 1	Months 2-8
Cycle duration, msec	990	1060	960
Mechanical systole, msec	344	355	338
Isometric contraction, msec	52	50	47
Ejection period, msec	291	302	290
Rapid ejection??, msec.	93	84	86
Diastole, msec	592	639	549
Isometric relaxation, msec	101	67	68
Rapid filling, msec	71	93	90
Auricular systole, msec	68	64	66
Slow filling, msec	454	487	305

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Diagram 2: Proposed schematic model of the mechanisms underlying changes in cardiac activity in response to provocative tests

Initial Hemodynamic State

Decreased volume of circulatory blood* and interstitial fluid*
 Increased blood volume in the cardiopulmonary region
 Decreased vascular tonus* and deconditioning of venous return mechanisms
 Increased compliance of the veins of the calves,* decreased muscle tonus and pressure of interstitial fluid in the region of the lower limbs
 Formation of zones of free venous compliance in the region of the calves (at rest there is no tension on the venous walls due to transmural pressure)

Mechanisms of Change In Response to LBNP and Exercise

LBNP

Greater shifting of blood from the cardiopulmonary region to the vessels of the decompression zone and greater increase in leg volume* than occurs on Earth

Greater decrease in venous return, stroke* and minute* blood volumes

Greater decrease in blood volume and pressure in the cardiopulmonary region and reflexive increase in adrenergic effects

Increased compensatory reactions in the form of greater increase in heart rate* and peripheral resistance*

Restructuring of phase structure of the cardiac cycle and development of myocardial hypodynamia syndrome due to establishment of different relationships among the major phases of the cycle*

Exercise

Greater redistribution of blood from the cardiopulmonary region to the venous bed of the legs than occurs on Earth

Less increase in venous return and stroke volume and increase in minute volume; primarily due to increased heart rate*

Greater decrease in blood volume and pressure in the cardiopulmonary region, and reflexive increase in adrenergic effects as well as direct activation of the sympathetic nervous system by exercise

Increased positive inotropic effects and production of catecholamines

Restructuring of cardiac cycle and development of myocardial hypodynamia syndrome (due to different relationships among phases of the cycle)*

*Space flight data

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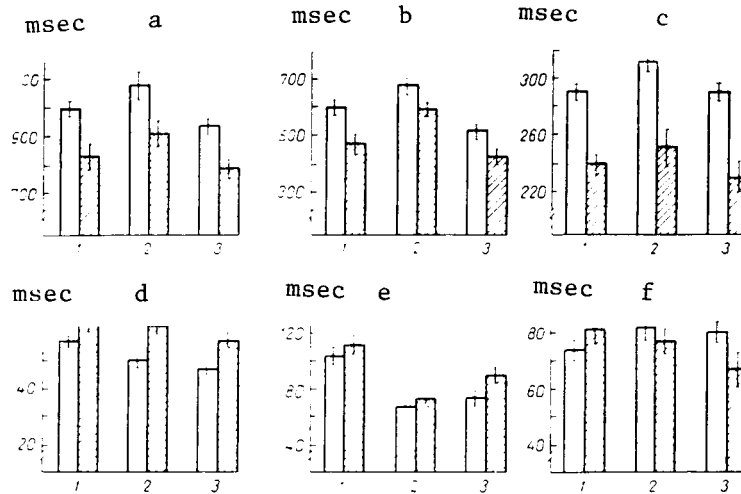


Figure 1: Dynamics of the major parameters of cardiac cycle phase structure in cosmonauts during 96-237 day flights on Salyut-6- and Salyut-7-Soyuz space station complexes in response to LBNP tests

Here and in Figure 2, a-e - cardiac cycle duration, diastole, ejection period, isometric contraction phase, isometric relaxation phase, and rapid filling phase; 1- preflight, 2 - month 1 of flight; 3 - months 2-8 of flight; white bars pre-LBNP; hatched bars - with decompression of -35 mm HG

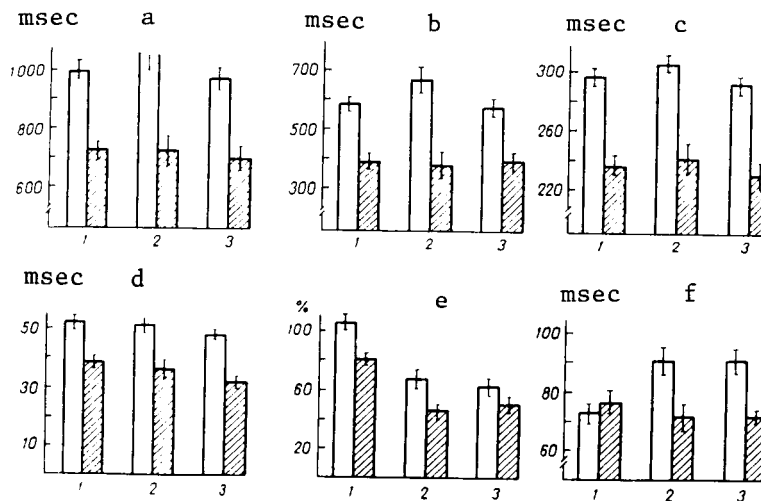


Figure 2: Changes in major parameters of cardiac cycle phase structure in cosmonauts during 96-237 day flight on the Salyut-6- and Salyut-7-Soyuz space station complexes in response to a graded physical exercise test

White bars-mean baseline values; hatched bars - mean values during minute 1 of the postexercise recovery period

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

P917(20/88)* Suvorov PM, Ivanchikov AP, Kondakov AV, Sidorova KA.
Investigation of hemodynamic response to a modified tilt test in individuals varying in their tolerance of $+G_z$ acceleration.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
22(4): 27-30; 1988.
[15 references; 4 in English]

Cardiovascular and Respiratory Systems, Hemodynamic Response
Humans, Individual Differences, Acceleration Tolerance
Tilt Test

Abstract: A modified tilt test, involving sequential upright and head-down tilt position combined with occlusion cuffs on the thigh has been proposed as an improvement over the traditional tilt test (passive upright position only) for purposes of predicting tolerance of $+G_z$ acceleration. This study attempted to compare hemodynamic responses to this modified tilt test (MTT) in individuals known to differ in their tolerance of $+G_z$. Subjects in the experiment were 40 pilots, aged 25 to 45. Testing on a centrifuge, revealed that 13 pilots had diminished tolerance of $+5G_z$ acceleration as assessed with standard criteria. Each subject underwent a traditional and a modified tilt test. The latter involved a 5-minute period in head down tilt position at an angle of -30° , followed by a shift to upright position with simultaneous inflation of the occlusion cuffs to a pressure of 100-110 mm Hg in experiment 1 and to 50 mm Hg in experiment 2. Time spent in upright position was 10 minutes. Occlusion cuffs were placed on the upper third of the thigh. EKG's were recorded during the tests using standard leads; changes in systolic and minute volumes of blood were registered using tetrapolar impedance plethysmography; while diastolic, mean dynamic, and true systolic blood pressure were measured using a tachoscillogram in the brachial artery. The following parameters of myocardial contractility were also measured: cardiac index, strength of contractions of the left ventricle, expenditure of cardiac energy to move 1 liter of blood, specific actual and working peripheral resistance, and arterial tonus stress. Data was analyzed using the t statistic and Pearson correlation coefficients.

In the first experiment (occlusion of 100-110 mm Hg in modified test), responses of hemodynamic parameters to upright position in the modified test was similar to that for a standard tilt test. These included a moderate, but significant, increase in heart rate and an increase in specific actual peripheral resistance, decrease in pulse blood pressure, systolic blood volume, and cardiac index, compared with baseline data measured in horizontal position. Cardiac index deficits during minutes 1-10 in the upright position were virtually identical in both tests (30.3 and 30.6%, respectively). Sinusoidal tachycardia and decrease in systolic blood volume were significantly greater in the traditional tilt test than in the modified one during the first minute in upright position. This difference was eliminated by minute 10. In both tests major hemodynamic parameters reflected a relatively high level of circulatory homeostasis, which was confirmed by the subjects' subjective assessments of their state. In general, no differences were found between response to the two tilt tests when the groups with high and low acceleration tolerance were considered separately. However, during minute 10 of the modified test, those with diminished tolerance displayed a small but significant decrease in mean blood pressure compared to that occurring in response to the traditional test.

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In the second experiment, where cuff pressure was 50 mm Hg in the modified test, no statistically significant differences were observed between parameters for the two tests. The authors conclude that the very slight differences between the two tests do not justify use of the modified procedure for predicting acceleration tolerance.

Table: Changes in major hemodynamic parameters in response to traditional and modified tilt tests

P921(20/88)* Vilkov VG, Shamarin VM. Shal'nova SA, Dmitriyeva VS.
The effect of exercise on changes in blood pressure, heart rate and electrocardiogram in upright position.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 43-47; 1988.

[23 references; 9 in English]

Cardiovascular and Respiratory Systems, Blood Pressure, Heart Rate, EKG
Humans, Males and Females, Patients, Hypertension, Ischemic Heart Disease
Exercise, Upright Position

Abstract: The goal of this work was to study how exercise affects the nature and extent of changes in cardiac parameters in response to assumption of an upright position. Subjects were 22 apparently healthy individuals (15 males and 7 females), 28 patients suffering from high blood pressure (19 males and 9 females), and 10 patients with chronic ischemic heart disease (6 males and 1 female). Mean age of the three groups was 44.1, 42.7 and 53.4, respectively. Subjects were required to perform graded submaximal exercise on a bicycle ergometer in horizontal position with work load increasing by 25 W every 3 minutes. Each subject was tested twice after assumption of upright position for 5 minutes, once before and once 6 minutes after exercising. EKG's were recorded from 12 traditional leads, systolic and diastolic blood pressure were measured, and heart rate was derived from EKG. Measurements were made during minutes 1 and 5 in the upright position before and after exercise, as well as before and after exercise in the horizontal position. Differences between baseline and post-exercise heart rate and systolic and diastolic pressures were computed for each of the two positions.

After exercise, upright position was associated with significant decreases in systolic blood pressure in all three groups. Before exercise this effect was only noticeable in hypertensive subjects. Diastolic blood pressure increased in healthy subjects in response to the upright position. In hypertensive patients, blood pressure did not change while they were in the upright position before exercise and increased after exercise. Subjects with high blood pressure showed lower blood pressure in horizontal position after exercising than before. Negative changes associated with upright position (e.g., depressed T wave and ST) were less pronounced after exercise than before in 50% of the subjects.

Table: Changes in blood pressure and heart rate in healthy individuals and subjects with high blood pressure and ischemic heart disease

Figure: EKG of subject K, 63 years old with 12 traditional leads

P934(20/88)* Vorob'yev VYe, Goncharov IB, Abdrakhmanov VR, Voronina SG.
Characteristics of changes in cardiac output and blood gases in humans exposed to simulated weightlessness.
 Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
 22(4): 94-96; 1988.
 [6 references; 3 in English]

Cardiovascular and Respiratory Systems, Cardiac Output, Blood Gases
 Humans, Males
 Hypokinesia with Head-Down Tilt, Long-Term

Abstract: This study compared changes in cardiac output measured using Fick's principle and in blood gases in humans undergoing long-term hypokinesia with head-down tilt. Twenty apparently healthy males participated in two experiments. Measurements were made during a baseline period before treatment and on days 30, 55, and 90 of a 120-day period of hypokinesia with head-down tilt (-40°). Samples of arterial blood were taken from the ulnar artery and analyzed immediately for partial oxygen and carbon dioxide pressure. Gas components of inspired and expired air were analyzed using a paramagnetic oxygen analyzer and an infrared CO_2 analyzer. results were used to compute the alveolar-arterial oxygen gradient. Minute ventilation was determined with a spirometer. Cardiac output was determined by measuring CO_2 pressure and oxygenation using rebreathing. Output was computed using the following formula:

$$Q_t = \frac{V\text{CO}_2}{C_v\text{-CO}_2 - C_a\text{CO}_2}$$

where Q_t is cardiac output (in l/min). $V\text{CO}_2$ is the amount of CO_2 expelled from the lungs (in ml/min) and $C_v\text{-CO}_2 - C_a\text{CO}_2$ is the vein-artery difference in CO_2 (in ml per 100 ml blood). All measurements were made while subjects were at rest (in a horizontal position during baseline, and in head-down tilt during treatment). Students' t was used to test significance of differences, and Spearman correlation coefficients were also computed.

On day 30 of hypokinesia, subjects showed a significant decrease in oxygen pressure in arterial blood and a simultaneous tendency for the alveolar-arterial oxygen gradient to increase. On day 55, CO_2 pressure increased as well. On days 55 and 90 of hypokinesia, the venous-arterial differences in CO_2 concentration were elevated, suggesting that insufficient alveolar ventilation may be responsible for some of the other effects. Cardiac output decreased reliably on days 30 and 55 of hypokinesia. The authors argue that decreased output in hypokinesia has a significant effect on the vein-artery difference in CO_2 pressure. Correlational analysis showed that during the first half of the hypokinesia period, there was a relatively close association between cardiac output and oxygen pressure in arterial blood. During the second half of hypokinesia, the size of the correlation decreased or even became negative in some subjects. The authors conclude that their results show that changes in CO_2 pressure in venous blood during exposure to hypokinesia with head-down tilt reflects the inadequacy of CO_2 -transport mechanisms, including alveolar ventilation, pulmonary gas exchange, cardiac output, and CO_2 transport. All these factors, not just alveolar ventilation, must be included when effects of this model are considered. Correlation analysis demonstrates the special importance of cardiac output.

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Table: Changes over time in parameters of cardiac output and blood gases in subjects exposed to hypokinesia with head-down tilt

M140(20/88) Yu. Vedru (editor).

Klinicheskiye, matematicheskiye i inzhenernyye problemy sportivnoy meditsiny
[Clinical, mathematical and engineering issues in sports medicine.

Tartu [Estonia]: Tartu State University [Press]: 1988.

Affiliation: Tartu State University

KEY WORDS: Cardiovascular and Respiratory Systems, Cardiac Volume, External Respiration, Operational Medicine, Exercise, Sports, Mathematical Modeling, Equipment and Instrumentation

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ENDOCRINOLOGY

(See also: Biological Rhythms M142; Immunology P913)

PAPERS:

P928(20/88)* Kirillov OI, Kurilenko LA.

The effect of long-term hypokinesia on the androgen system of rats.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 74-76; 1988.

[20 references; 11 in English]

Endocrinology, Androgen System, Reproductive Biology
Rats, Male
Immobilization, Cages

Abstract: Male Wistar rats with initial body weight of 145-155 were placed in immobilization cages. Control rats were housed in normal cages. Eight rats from each group were sacrificed after 1, 5, 10, 15, 20, 30, 45, 60, and 90 days and their testes, seminal vesicles, and prostate glands were extracted and weighed. The left adrenal was fixed in Carnoy's fixative and poured into paraffin. Sections were produced and stained with hematoxylin and eosin. From each section, 200 nuclei from the reticular zone were traced at a magnification of 1200; nuclei were measured and volumes computed. Significance was tested using t-tests with a significance criterion of $p \leq 0.001$ for nuclei volume and $p < 0.05$ for the remaining parameters. Log transforms were apparently used in some or all cases.

During the 90-day period, the body weights of control rats more than doubled. During the early (< 30 days) hypokinesia period, growth of experimental rats was retarded relative to controls and then began to decrease to below baseline. The weight of the seminal vesicles and prostate gland increased by a factor of 2.7 in control animals. In immobilized rats, the weight of the vesicles and prostate decreased reliably after 5 days of treatment. On days 45 and 60, these organs weighed less than half those of the controls. While testes weight was below that of controls throughout the experiment, the difference was never statistically significant. The authors postulate that an increase in the level of 5 alpha-dehydrotestosterone in plasma, associated with stress, maintained testes weight. In immobilized rats, the volume of cell nuclei was significantly higher than in control rats on days 1 and 5 of treatment. During days 10 and 15, the difference was no longer significant. And on days 20 and subsequently, nuclei volume decreased progressively in experimental animals.

The authors conclude that the responses of various components of the androgenic system to long-term hypokinesia are different. The greatest change is a decrease in the weight of the seminal vesicles and prostate. The cell nuclei in the reticular zone of the adrenal cortex undergo hypertrophy during the early immobilization period, which is likely to be associated with stimulation by corticosterone rather than androgens. Later in the hypokinesia treatment the volume of cell nuclei in the reticular zone decreased below control level. This phenomenon is likely to be significant for maintaining reproductive function.

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Table: Volume of cell nuclei in the reticular zone of the adrenal cortex in control rats and rats subjected to hypokinesia

Figure: Weight of body, seminal vesicles and prostate gland, and testes in control rats and rats subject to hypokinesia.

ENZYMOLGY

(See also: Biological Rhythms M142; Neurophysiology P942)

PAPERS:

P927(20/88)* Vetrova YeG, Drozdova TYe, Popova IA.

The effect of horizontal hypokinesia and hypokinesia with head-down tilt on activity of serum enzymes.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 70--73; 1988.

[16 references; 2 in English]

Enzymology, Hematology, Serum Enzymes

Humans, Males

Hypokinesia, Bed Rest, Horizontal, Head-Down Tilt

Abstract: The goal of this work was to investigate the activity of a number of human serum catabolic and transamination enzymes under conditions of weightlessness as simulated by hypokinesia with varying angles of head-down tilt and under exposure to emotional stress. Subjects were 10 healthy male volunteers, of whom 5 were subjected to a 7-day period of bed rest in a horizontal position (group 1) and 5 to a head-down position (-6°) (group 2). Blood was taken from fasting subjects in a supine position from the ulnar vein on days 6, 12, and 14 before beginning treatment; on days 2, 4, and 7 of bed rest; and on days 2 and 7 of a recovery period. Enzymes studied included malate dehydrogenase, isocitrate dehydrogenase, lactate dehydrogenase, alanine aminotransferase, and creatine kinase and its isoenzymes. Activity levels were determined with a standard set of reagents. Isoenzymes of malate and lactate dehydrogenase were studied using electrophoresis in a polyacrylamide gel. Effects of emotional stress on activity of isocitrate, malate dehydrogenase, creatine kinase and the distribution of malate dehydrogenase isoenzymes, was studied in male students who had just taken a university entrance examination. Blood was taken from the ulnar vein immediately before this beginning of the examination and immediately afterward. Student's *t* was used to determine statistical reliability.

All parameters measured were within normal limits before the study. Beginning on day 2 of hypokinesia, there was a gradual decrease in activity of malate and isocitrate dehydrogenase of 25 and 29%, respectively in group 1, and 19 and 20% respectively in group 2. Minima were reached on day 7 of treatment. During the recovery period, isocitrate dehydrogenase normalized on day 2, and malate dehydrogenase on day 7. No significant changes were observed in lactate dehydrogenase, alanine dehydrogenase, aspartate amino transferase, or in distribution of isoenzymes of malate and lactate dehydrogenase. By day 2, creatine kinase activity had increased by 38% for group 1 and by 29% in group 2 due to a one-time increase in muscle and myocardial isoforms. Subsequently, on days 4 and 7, these levels dropped to below baseline. This decrease was statistically significant for group 1. By day 7 of readaptation, activity of creatine kinase and its isoenzymes had returned to baseline. Initial increase in this activity in hypokinesia is attributed to a stress reaction. Thus the enzyme activity changes occurring in response to the two different models of hypokinesia involve only malate and isocitrate dehydrogenase, which act to transform the substrate of

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oxidative metabolism into the Krebs cycle, and creatine kinase, which catalyzes the resynthesis of ATP by transforming creatine phosphate. Significant changes in these enzymes were not noted in connection with the stress paradigm.

The authors conclude that the decrease in activity of serum enzymes that occurs in response to hypokinesia and recovers rapidly after its termination reflects depressed energy utilization, is not related to hemodynamic changes or emotional stress, and is mainly adaptive in nature and specific to motion deficit.

Table 1: Activity of enzymes and distribution of isoenzymes in blood serum during horizontal hypokinesia

Table 2: Activity of enzymes and distribution of isoenzymes in blood serum in hypokinesia with head-down tilt

Table 3: Activity of enzymes and distribution of isoenzymes in blood serum in response to emotional stress

EXO BIOLOGY

PAPER:

P941(20/88) Chetkauskayte AV, Grinyus LL, Mukhin LM.

The stimulating effects of polyphosphates on the formation of peptides from glycine and phenylalanine amine under abiogenic conditions.

Zhurnal Evolyutsionnoy Biokhimii i Fiziologii.

XXIV(4): 465-470; 1988.

[17 references; 14 in English]

Exobiology, Abiogenic Synthesis

Peptides

Polyphosphates

Abstract: The goal of this experiment was to determine if polyphosphates can serve as an energy source in reactions when peptides form from amides of amino acids. Glycine amide (GlyNH_2) and phenylalanine amide (PheHG_2) were synthesized in the laboratory. The reaction mixture (final volume 0.1-0.25) was prepared by dissolving the glycine or phenylalanine amides to a final concentration of 50 mM in a medium containing 0.3M imidazol (pH 10.0). The medium additionally contained 0.1M pyrophosphate or tripolyphosphate or 10.2 mg Graham's salts in 1 ml. The pH of the reaction mixture was 10.0, with the exception of the experiment where the effect of Ca^{++} on the polymerization process was studied, and pH was 7.0 to prevent Ca^{++} precipitation. The reaction took place in sealed ampuls over a period of 12 days at different temperatures. Polymerization products were analyzed using horizontal electrophoresis in a 0.03M triethylamine-bicarbonate buffer with pH of 7.0 at 1300 V for 35 minutes on FN2 chromatographic paper, which had first been washed in 1N HCl and water until it reached a neutral pH. Gly-gly was used to calibrate the instruments. The electrophoregram was fixed with a 0.5% solution of ninhydrin in acetone in the presence of 1% volume of 96% acetic acid and 5% water, incubated for 5 minutes at 20°C and then left at 60°C for 30 minutes. The color indicators were cut out and eluted for 3 hours in the dark by 80% ethanol, containing cupric nitric acid. Optical density of the eluate was determined spectrophotometrically at 510 nm. To determine the amino acid composition of the products, the eluate was boiled dry and the precipitate suspended in 6N of hydrochloric acid and incubated for 24 hours at 110°C. The hydrochloric acid was boiled and the precipitate washed to neutral pH and analyzed in a butanol-acetic acid-water system (4:1:1). Amino acids were detected with ninhydrin at 60°C. Liquid column chromatography of the polymerization products was performed on a column filled with sephadex G-10. The column was washed with water at a rate of 8.4 ml/hour and the optical densities of the liquids produced were recorded at 252 nm. The amount of orthophosphate was determined in the presence of labile phosphate esters or high concentrations of ATP before and after polymerization of GlyNH_2 . Mean deviation was determined for the results of three parallel studies.

Electrophoretic analysis showed that when GlyNH_2 was polymerized, substances formed which could be distinguished by their electrophoretic mobility. In the absence of Graham's salts in the medium, substances with low mobility predominated. When the salts were present, additional substance

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substances with higher mobility formed. When the products were analyzed the profile of the more mobile products showed the presence of one major and two minor peaks. Analysis revealed a background quantity of GlyNH₂ for all peaks, while the major peak contained Gly-Gly and traces of Gly-Gly-Gly. When the fractions in the main peak were boiled dry and hydrolyzed, only Gly was observed. Study of GlyNH₂ in a wide temperature range showed the stimulating effect of Graham's salts (total yield was 75% with the salts, 45% without them). If Graham's salts were present, the optimum temperature for Gly-Gly formation was 30-40° C (in the absence of the salts the optimum was 50-80° C). The maximum yield of other oligopeptides occurred at 20° C. The total yield of oligopeptides reached 75%. The stimulating effect of Graham's salts occurred at 2 pH intervals: 6-10 and 3-2. Maximum peptide yield occurred at pH of 10. In addition to Graham's salts, tripolyphosphate and pyrophosphate also stimulated production of Gly-Gly. The amount of Gly-Gly formed far exceeded the amount of inorganic polyphosphates.

In study of polymerization of PhenH₂, it was found that in decomposition of tripolyphosphate, the amount of orthophosphate produced was approximately equal to that of oligopeptide, while in a mixture containing Graham's salts the production of orthophosphates was greater. No correlation was found between the production of oligopeptides and orthophosphate in observations of the effects of Ca⁺⁺ on GlyNH₂ polymerization. Introduction of Ca⁺⁺ led to a decrease in yield of Gly-Gly when the mixture contained Graham's salts and tripolyphosphates. However, in the presence of pyrophosphates the yield of Gly-Gly increased when calcium was added.

The authors conclude that Graham's salts, tripolyphosphate and pyrophosphate can act as catalysts for the formation of peptides from the corresponding amino acid amides in a homogeneous medium.

Table 1: The effects of polyphosphates on polymerization of GlyNH₂

Inorganic polyphosphate in medium	Gly-Gly	Yield (mM)	
		P _i	
		Method 1	Method 2
Absent	4.7	0.0	0.0
Pyrophosphate	12.0	0.0	0.0
Tripolyphosphate	14.3	8.2	6.9
Graham's salts	4.8	6.0	5.9

Table 2: The effects of polyphosphates on polymerization of PhenH₂

Inorganic polyphosphate in medium	oligopeptides	Yield (mM)	
		P _i	
		Method 1	Method 2
Absent	1.6	0.0	0.0
Pyrophosphate	4.9	1.6	3.0
Tripolyphosphate	2.9	3.3	3.7
Graham's salts	1.5	2.5	4.5

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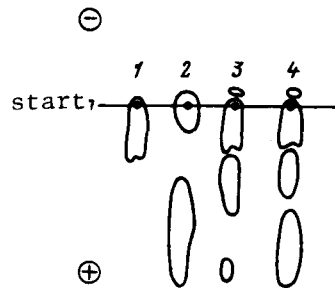


Figure 1: Electrophoregram of products of GlyNH₂ polymerization
 On the start line: 1 - 500 nmole glyNH₂, 2 - 50 nmole
 Gly-Gly, 3.4 - 10 ul each polymerization products. In 4 the
 polymerization occurred in the presence of Graham's salt. Polymerization
 temperature: 20° C

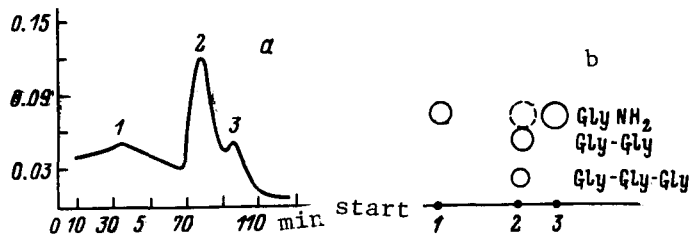


Figure 2: Purification of products of polymerization of GlyNH₂ on sephadex
 G-10 (1) and analysis by TCX method (b).

A - optical density at wavelength 252 nm, B - elution volume (ml).

On the start line: 2 um each of 50 times concentrated eluate of products
 of polymerization from peaks 1, 2, 3. Polymerization occurred at 50° C in
 the presence of Graham's salts.

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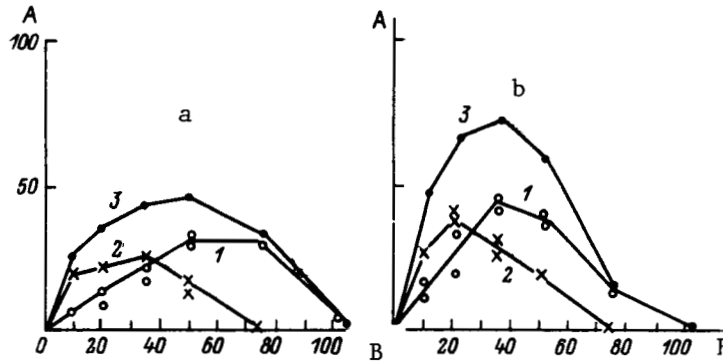


Figure 3: Yield of polymerization of GlyNH₂ in the absence (a) and presence (b) of Graham's salts at different temperatures.

A - yield of oligopeptides in polymerization (%), B - temperature of polymerization (°C). a - yield of Gly-Gly, b - yield of other oligopeptides, 3 - total yield of peptides.

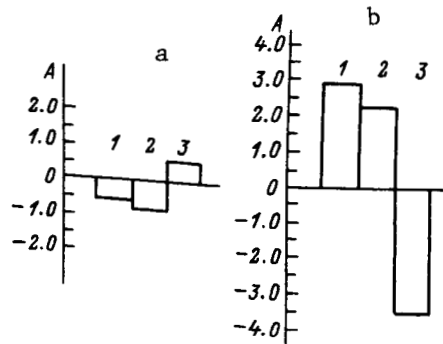


Figure 4: Effect of Ca⁺⁺ on yield of Gly-Gly (a) and formation of P_i (b) in polymerization of GlyNH₂.

A - change in yield of Gly-Gly (mM, a) or formation of P_i (mM, b) with Ca⁺⁺ in the medium, containing in addition: 1 - Graham's salts, 2 - tripolyphosphate, CaCl₂ added for a final concentration of 10mM.

GASTROINTESTINAL SYSTEM: See Biological Rhythms: M142
GENETICS: See Immunology M139
HABITABILITY AND ENVIRONMENT EFFECTS: See Operational Medicine P910

HEMATOLOGY

(See also: Biological Rhythms M142; Enzymology P927;
Musculoskeletal System P925)

PAPER:

P943(20/88) Gol'dberg YeD, Zakharova OYu, Dygay AM.

Modulating effect of opioid peptides on hemopoiesis in stress.

Byulleten' Eksperimental'noy Biologii i Meditsiny.

CVI(7): 23-26; 1988

Hematology, Hemopoiesis

Mice, Males

Immobilization Stress, Opioid Peptides, Lev-Enkephalin

Abstract: The goal of this work was to determine the effect of certain opioid peptides, lev-enkephalin and its synthetic analogue, dalargin, on response of the blood system to immobilization stress varying in duration. Experiments were performed on 500 outbred male mice subjected to 6-hours [daily?? authors do not specify] of immobilization on their backs followed by a single intraperitoneal injection of lev-enkephalin or dalargin in a dose of 100 ug/kg. A control group also underwent immobilization, but received only isotonic saline. Material for study was taken at various periods after treatment began (up to 10 days). The quantity and types of cells in peripheral blood (leukocytes, erythrocytes, and reticulocytes) were determined, as was the total number of myelokaryocytes (in the femur). Smears of bone marrow were used to obtain a myelogram. Mitotic activity of bone marrow cellular elements was evaluated statokinetically. Two hours before sacrifice mice were given intraperitoneal injections of colchicine in a dose of 4 mg/kg. The statokinetic index was computed per 1000 erythrocyte and granulocyte hemopoietic cells potentially able to divide. Concentration of 11-OCS was determined fluorometrically.

One day after immobilization, the animals showed signs of developing the characteristic blood systems redistributive reactions. Three hours after the beginning of treatment, neutrophilic leukocytosis developed with an increased number (191% baseline) of neutrophils with segmented nuclei. The number of eosinophils decreased and completely disappeared after 12 hours. A "lymphoid peak" was noted in bone marrow after 3 hours, with number of lymphoid cells reaching 233% of baseline, while lymphopenia developed in peripheral blood. All these parameters returned to normal within a day after immobilization began. A single administration of lev-enkephalin or dalargin prevented development of early lymphopenia and decreased eosinophilia.

On day 6-8 of immobilization, control animals developed marked hyperplasia of bone marrow. Total number of myelokaryocytes reached a maximum (140% of baseline) at 7 days. The myelograms showed that increased number of cells in marrow was due to stimulation of erythro- and granulocytopoiesis to 245 and 140% of baseline, respectively. Peripheral blood was characterized by neutrophilic leukocytosis, monocytosis,

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erythrocytosis, and reticulocytosis. In experimental animals, lev-enkephalin decreased bone marrow hyperplasia in immobilized animals while dalargin led to the development of hypoplasia of bone marrow hemopoiesis on days 6-8. This suppression of hemopoiesis altered the dynamics of cell distribution in peripheral blood. Both drugs prevented development of neutrophilic leukocytosis, monocytosis and erythrocytosis, and dalargin prevented an increase in reticulocytes. Immobilization stimulated mitotic activity of granulocyte cells, which increased to 133% baseline on day 6-7. Lev-enkephalin decreased the number of proliferating cells, while dalargin inhibited the increase in mitotic activity of hemopoietic elements. The statokinetic index in the group injected with dalargin did not differ from preimmobilization value. Immobilized mice showed a pronounced increase in concentration in plasma corticosteroids hours after treatment began, followed by cyclic fluctuations; this parameter remained elevated until day 3 of the experiment. Animals receiving dalargin showed no such increases; 11-OCS levels were below baseline. [Effects of lev-enkephalin are not described; possibly not tested.] The authors conclude that the effect of opioids on hemopoiesis in bone marrow under stress is mediated by their depression of the pituitary-adrenal system, which leads to a decrease in the proliferative capacity of bone marrow elements and alters the hemopoietic component of the general adaptation syndrome.

Table: Concentration of 11-OCS in plasma of outbred mice subjected to a 7-hour period of immobilization followed by administration of isotonic saline or dalargin

Figure 1: Changes in the total number of myelokaryocytes, erythroid cells, and immature neutrophilic granulocytes in bone marrow of outbred mice subjected to 6 hours of immobilization followed by injection of isotonic saline, lev-enkephalin, or dalargin

Figure 2: Changes in mitotic activity of cells of erythroid and granulocytary elements of hemopoiesis in outbred mice subjected to 6 hours of immobilization followed by injection of isotonic saline, lev-enkephalin, or dalargin

HUMAN PERFORMANCE: See Adaptation M141, Operational Medicine P910

IMMUNOLOGY

PAPERS:

P908(20/88) Kuznets YeI, Kut'kova ON, Yakovleva EV, Shal'nova GA, Malkiman II, Yastrebov PT.

Selection of parameters indicative of human immune status under conditions simulating space flight factors.

In: Malinin VB, Kosmolinskiy FP, Kuznets YeI (editors).

Perspektivy Razvitiya Kosmicheskoy Biomeditsiny v Svete Idey K.E.

Tsiolkovskiyogo [Prospects for the Development of Space Biomedicine in Light of the Ideas of K.E. Tsiolkovskiy] Proceedings of the XXth and XXIst Lecture Series dedicated to the scientific legacy and development of the ideas of K.E. Tsiolkovskiy., Kaluga 1985, 1988. Section on Problems of Space Medicine and Biology.

Moscow: USSR Academy of Sciences: 1987.

Pages 101-105.

[7 references; none in English]

Immunology, Immune Status

Humans

Heat, Hypokinesia With Head-Down Tilt, Hermetically Sealed Living Quarters

The problem of maintaining high work capacity and tolerance of adverse environmental factors in spacecraft crews was one of K.E. Tsiolkovskiy's enduring research interests. The solution of this problem at the current stage in the development of cosmonautics is associated with the use of the results of ground-based biomedical experiments simulating space flight factors.

Discovery of the mechanisms underlying adaptive restructuring in the human body in response to space flight factors is not possible without information concerning immune status.

From the point of view of general biology, the function of natural immunity involves the capacity to retain useful information acquired through evolution and necessary for vital processes in the face of changes in living conditions. Evaluation of this capacity by investigating the most labile parameters of natural immunity is an essential aid in diagnosing and predicting functional state and assessing the physiological cost of maintaining homeostasis during space flight. The current experiments involved selecting the immunological parameters that provide the most information for diagnosing and predicting human functional status under exposure to simulations of space flight factors combined with thermal stress. Healthy male volunteers, aged 19-35, participated in three conditions. In the first condition, the volunteers were subjected to heat ($T^0 = 50$; $\varphi = 25\%$) up to the maximum acceptable level of heat stress. In the second condition, the volunteers spent 10 days in a hermetically sealed environment in a comfortable microclimate. Every day they spent 2 hours performing moderate physical exercise, and the next day were subjected to heat ($T = 40^0$; $\varphi = 30\%$). In the third condition, the subjects spent 7 days in hypokinesia with head-down tilt (-8^0), simulating the acute period of

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adaptation to weightlessness. On days 3, 5, and 7, they were subjected to thermal stress ($T=50^{\circ}$; $\varphi = 25\%$) until rectal temperature increased by 1.0° .

During the experiment, in addition to physiological parameters, the following immunological parameters were measured: phagocytic activity of neutrophils; lysozyme titers in saliva; level of spontaneous agglomeration of leukocytes; activity of beta-lysines; bacterial activity of blood serum; class A, M, and S immunoglobulins; S-reactivity of proteins; quantity of T- and B-lymphocytes; and also density of deep microflora of the skin. Only parameters showing statistically significant differences from baseline values ($p < 0.05$) were considered.

Taxonomic analysis of the effects of the first condition (22 observations) made it possible to separate the volunteers into two groups on the basis of type of response to heat stress: tolerant and less tolerant. The period of endurance of thermal stress for the two groups was 181.1 ± 19.1 and 126.1 ± 8.7 minutes, respectively. The baseline values of a number of immunological parameters were significantly higher in the heat-tolerant group (phagocyte response to neutrophil - $48.4 \pm 1\%$; lysozyme titer in saliva - $225.3 \pm \text{ug/ml}$) compared with those of the less tolerant group (41.4 ± 1.5 ; $198.9 \pm 9.7 \text{ ug/ml}$). Aside from their prognostic value, these parameters are informative with regard to diagnosis of functional state after thermal stress. Thus, if thermal stress increased phagocytosis and lysozyme output in both groups, only in the tolerant group were these parameters still elevated and microbial population of the skin normal 20 hours after heat stress. This suggests an adequate response to increased tissue metabolism during and after thermal stress. At the same time, decrease in phagocytic activity of neutrophils and lysozyme titer in saliva and high levels of microbes on the skin observed in the less tolerant group, indirectly suggests poor endurance of heat stress. The latter hypothesis is confirmed by the neutrophilia (6.8 ± 2.3 thousand/ μm^3) and eosinopenia ($0.8 \pm 1.0\%$) observed in this group.

Shifts in immunological parameters in 6 subjects spending time in a hermetically sealed environment and exposed to thermal stress (condition 2), occurred after 6-10 days: both cellular (phagocytic activity of neutrophils - decreased from 48.5 ± 2.2 to $29.5 \pm 1.8\%$) and humoral (lysozyme titer of saliva decreased from 251.6 ± 33.8 to $148.5 \pm 30.5 \text{ ug/ml}$) nonspecific immunity were depressed and stress increased in the leukocyte system (level of spontaneous agglomeration of leukocytes increased from 1.6 ± 0.3 to $4.0 \pm 0.3\%$), and skin microflora increased from 24.0 ± 9.5 to 114.5 ± 3 colonies per 10 cm^2 . These changes occurred against a background of neutrophilia and eosinopenia, supporting a hypothesis of activation of the hypothalamus-pituitary-corticoid system in response to the stress factor. This would lead to the observed decrease in nonspecific tolerance and the risk of autoimmune disorders.

The combination of hypokinesia with head-down tilt and heat stress (condition 3, 36 subjects) after 3-7 days of exposure depressed nonspecific immunity. The longer the exposure to hypokinesia, the greater were the decreases in phagocytic activity of neutrophils (from $42.8 \pm 1.0\%$ to $21.5 \pm 2.5\%$), lysozyme titers in saliva (from 225.0 ± 11.2 to $151.2 \pm 14.7 \text{ uk/ml}$)

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and the increase in skin microflora (from 26.9 ± 5.7 to 70.9 ± 22.1). By day 5-7, the disturbance of the antimicrobial component was accompanied by destruction of the autoimmune component, an increase in the activity of Beta-lysines (from 19.3 ± 3.8 to $34 \pm 1.1\%$) and level of spontaneous agglomeration of leukocytes (from 2.6 ± 0.5 to $7.3 \pm 0.4\%$). The severity of the state of the organism was confirmed by disruption of the T-system of immunity. Thus, the quantity of T-lymphocytes decreased from 61.4 ± 2.0 to $17.4 \pm 3.3\%$.

The research performed demonstrated that the immune system is a sensitive indicator of adaptive restructuring occurring in the body in response to simulated space flight factors. Selection of the most informative immune parameters for assessing and predicting functional state of the human organism must take account of the severity and duration of exposure to the extreme factor.

Therefore, to diagnose and predict endurance of thermal stress per se and combined with short-term confinement in a hermetically sealed environment (no longer than 10 days) or exposure to hypokinesia (for no longer than 2-3 days), the following immune parameters are recommended: phagocytic activity of neutrophils, lysozyme titers in saliva, level of spontaneous agglomeration of leukocytes, and deep skin microflora.

When greater stress is applied, the above list of parameters should be supplemented by study of the T-system of immunity and autoimmunity.

P913(20/88) Priyatkin SA, Morozov VI, Rogozkin VA.

The effect of physical exercise on nonspecific resistance factors and concentration of steroid hormones in human blood.

Fiziologiya Cheloveka.

14(4): 606-613; 1988.

[35 references; 10 in English]

Authors' Affiliation: Scientific Research Institute of Physical Culture, Leningrad

Immunology, Nonspecific Resistance; Endocrinology, Steroids
Humans, Males, Athletes
Exercise

Abstract: The goals of this study were to determine the effects of a single strenuous exercise session on cellular and humoral nonspecific resistance and also to investigate the possible participation of steroid hormones in regulation of nonspecific resistance factors. A total of 72 male athletes (rowers), aged 17 to 23, participated in the study. The exercise used was running on a treadmill until exhaustion (mean duration 17 minutes). Nonspecific resistance parameters and concentration of steroid hormones were measured before and immediately after exercising. In half of the subjects, parameters were also measured during the ninth minute of exercise and 0.5, 1, and 2 hours afterward. Functional status of neutrophils was evaluated on the basis of the mean cytochemical coefficient reflecting concentration of lysozomal cation proteins in these cells. Concentration of lysozyme was determined using a modified turbidimetric method. Complement titers were estimated from 50% hemolysis of sheep erythrocytes. Concentration of leukocytes in blood and of various types of white blood cells were also determined. Serum testosterone, estradiol, and hydrocortisone were determined by radioimmune assay.

The exercise treatment led to a two-phase change in the level of leukocytes in peripheral blood in all subjects. Immediately after exercise, the absolute level increased by a mean of 66%, with neutrophils increasing by 46%, lymphocytes by 113%, and monocytes by 85% of baseline values. After 30 minutes all these parameters had returned to their initial values. One hour after exercise there was a second increase in leukocytes, this time attributable only to a 68% rise in neutrophils (lymphocytes decreased by 43% and monocytes were unchanged). After 2 hours of rest there was a further increase (77%) in leukocytes, again due only to neutrophils. At this time, there was also a fourfold increase in immature neutrophils, while lymphocytes continued to be below baseline. The great majority of subjects displayed a decrease in the mean cytochemical coefficient of neutrophils after exercise, indicating a decrease in lysozomal cation proteins. At the same time, concentration of lysozyme (one of the lysosomal cation proteins) increased in serum, evidently due to secretion by the cells. The complement system responded rapidly to exercise; as early as the 9th minute of treatment, there was a 19% increase in complement titer. By the second hour after treatment, the mean cytochemical coefficient of neutrophils and the activity of lysozyme and complement in serum had completely or partially recovered in most subjects.

Immediately after exercise, concentration of estradiol increased by 20%; after 30 minutes it returned to baseline, and again increased by 30% after 2 hours. Testosterone increased during exercise, and at its

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termination was 28% above baseline. During the next 2 hours testosterone rapidly normalized. Hydrocortisone behaved differently in different subjects. In one group, which had low baseline levels of the hormone, it increased rapidly in serum during exercise. Maximum concentration, 77% above baseline, was reached after 30 minutes, after which the level returned to normal. In the second group, with high initial hydrocortisone levels, there was a tendency for the hormone to decrease during exercise, increase after 30 minutes of rest, and then undergo a more extreme decrease (by 51% compared to baseline) at the end of the observation period.

The authors conclude that nonspecific resistance factors, particularly neutrophils, respond actively to physical exercise. One of the symptoms of this response is the increased secretion of enzymatic and nonenzymatic lysosomal proteins, which may participate in the regulation of structural homeostasis and contribute to temporary adaptation to exercise. This response of the nonspecific resistance system is universal and serves, possibly, to repair various types of damage, particularly elimination of the damaged structures. At the same time, the sex steroids are recruited in the regulation of the functional activity of nonspecific resistance factors.

Figure 1: Changes in blood concentrations of lymphocytes (1), neutrophils with segmented nuclei (2), basillary neutrophils (3), and monocytes (4)

Figure 2: Changes in mean cytochemical coefficient of neutrophils, and lysozymes and complement in blood serum

Figure 3: Changes in concentration of testosterone, estradiol, and hydrocortisone in blood serum

MONOGRAPH:

M139(20/88) Petrov RV, Lozovoy VP.

Problemy i perspektivy sovremennoy immunologii. Metodologicheskii analiz [**Problems and prospects of modern immunology. A methodological analysis**].

Novosibirsk: Nauka; 1988.

[256 pages]

Affiliation (book): Siberian Division USSR Academy of Sciences; Institute of Clinical Immunology, Siberian Division, USSR Academy of Medicine.

KEY WORDS: Immunology, Neurophysiology, Endocrinology, Aging, Immune Surveillance, Genetics

Annotation: This collection is devoted to analysis of modern trends in immunology. Problems of immunity and aging and the interrelationship between the neural, endocrine, and immune systems are discussed from a theoretical standpoint. The concept of immunological surveillance, including monitoring of cell differentiation, is considered. The origin of the immune system and the general principles of its organization are also covered. This book will be of interest to immunologists, biologists, and oncologists.

Contents

V.P. Lozovoy. **Methodological aspects of modern clinical immunology (principles for studying the immune function in the norm and pathology)** (3)

This paper presents an analysis of the state of the art in clinical immunology. The author formulates the basic methodological principles for evaluating new scientific facts and drawing conclusions from them in order to further understand the role of immune process in pathology. These principles involve a systems approach and use of systems analysis methods. These principles must account for the following phenomena: the cyclic nature of immune functions and their division into discrete phases; the age-linked characteristics of immune system physiology and pathology; the adequacy of an immune system response to the body's "demands;" the obligatory participation of the immune system in standard pathological processes; and the existence of individual differences in the way the immune system is structured. The author cites examples to support his conclusions and discusses the significance of these methodological principles for the development of clinical immunology.

O.K. Baranov. **Molecular genetic systems of immunological recognition.** (14)

This article considers the three most important genetic systems (multigene families) of immunological receptors: the major tissue compatibility complex, immunoglobulins, and T-cell receptors. The unique and common features of the structure and functions of various immunological receptors are described, as are the organization and restructuring of genes in the appropriate multigene families. The author touches upon the problem of the marked variety of immunological receptors, the significance of this phenomenon for selection, and the evolutionary and genetic mechanisms that underlie it. He discusses the homology and common phylogenetic origin of immunological receptors and their genes. The three molecular-genetic

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systems considered are the principal members of a single supergene family of immunoglobulin-like glycoprotein molecules, which in a unique manner provide genetic information to support the fundamental immunological processes of specific recognition and binding of a large number of antibodies. [1 table, 6 figures, 28 references]

G.M. Butenko, G.M. Kharazi. Methodological approaches to the study of the immune system with aging. [35]

The authors analyze problems of changes in the functions of the immune system with age. They emphasize that these functions change in different directions in different strains of inbred mice. They advance a hypothesis to explain this difference in direction, postulating the existence of two basic types of change in the immune system with aging: autoimmune and immune-suppressor. They propose the use of this taxonomy for development of principles for correcting immune disorders associated with aging. [29 references]

I.M. Dizmorov, V.A. Kuznetsov. The role of cellular ratios in supporting physiological homeostasis. (43)

The authors present various approaches to study of the role of cells that regulate the effector stage of the cellular immunity response and participate in immunological surveillance. The mathematical simulation of the processes of kinetic analysis and analysis of the limiting dilution type leads the authors to the conclusion that the distributions of interacting cells of the immune system determine not only the magnitude, but also the direction of the effect produced. These principles can be seen in the well-known paradoxical phenomenon of anti-tumor immunity -- the phenomena of stimulation and slipping??. [9 figures, 45 references].

V.A. Kozlov. The evolutionary basis of the functions of the "immune system." (66)

The author attempts to assess the significance of the immune system in the organism from the point of view of its polyfunctionality, in which the struggle to maintain "antigenic" purity in a macroorganism is only one of several functions of the given homeostatic system. To achieve this goal he uses an evolutionary approach which is based on the most primitive function of any cell - the capacity for phagocytosis of active substances needed for the optimal functioning of homeostasis. [11 reference]

V.I. Konenkov, M.I. Musatov. The mobility of human membrane proteins as a factor in activity of cells of the immune system. (74)

Data on the variability of expression of membrane proteins of lymphocytes, their production in an extracellular medium and their reabsorption are considered from the point of view of general cytophysiological and chronobiological principles. It is demonstrated that the variety of surface structure is associated with the fluidity of the bilipid layer or the state of the contractile apparatus of the cell, and has an important influence on such crucial immune cell functions as the capacity to interact with each other, recognize alien cells and antigens, effect

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lysis on target tumor cells, etc. The sequential changes in surface determinants follow ordered high frequency (bio)rhythms and combine into compact agglomerates on lymphocyte membranes. Production-reabsorption processes of the surface molecules and the degree of their expression on lymphocyte membranes also are subject to biorhythms. Changes in membrane topography of surface glycoproteins are closely linked with changes in the level of their expression, which are reflected in the functional activity of the cells. The immunological phenomena discussed accord well with the concept of membrane circulation. [3 figures, 33 references]

Ye.A. Korneva, M.P. Lesnikova, Ye. E. Yakovleva. Molecular biological aspects of the study of the interactions of the neural, endocrine, and immune systems. (87)

This article considers the potential for research on the interaction of neural endocrine and antigen factors at the level of the receptor apparatus of the lymphoid cells. The primary methodological strategy is determination of the level of cyclic nucleotides in lymphocytes of the spleen under conditions of exposure to antigens, hormones, neuromediators, and preparations blocking or stimulating their effects, and also the study of specific functions of lymphoid cells in animals immunized in vivo under a variety of endocrine status conditions and in in vitro experiments in which cholinergic substances are added to the culture during the period of active immune response. A correlation was found between the level of cyclase systems of lymphoid cells and the functional activity of these cells. Corrective neural and endocrine effects were demonstrated under in vivo and in vitro conditions, demonstrating the significance of endocrine and neuromediator mechanisms in the modulation of functions of lymphoid cells.

This work presents one of the new important methodological approaches to the study of problems of neurohumoral regulation of the functions of the immune system, which has made it possible to begin to investigate the realization of neural and endocrine correction and identify the mechanisms responsible for maintaining the linkages between the balance of mediators, glucocorticoid hormones, metabolic shifts in lymphoid cells, and their functional activity. [2 tables, 6 figures, 28 references].

G.I. Marchuk, R.V. Petrov. Viral infection of an organ and the immunophysiological protection response (a mathematical model). (100)

This paper presents a mathematical model of antiviral reactions of the immune system in an organ infected with a virus. The model includes a number of physiological parameters: the functions of killer cells, antibodies, and the degree of edema in the affected organ. In the mathematical analysis performed specific problems were formulated for experimental research to confirm the reliability of the results obtained through modeling. (1 figure)

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N.V. Medunyt'sin, O.R. Krylov, N.A. Alpatova, Zh.I. Avdeyeva. **Modeling reactions of delayed type hypersensitivity in vitro.** (108)

Data are presented on the modeling of the immune response in vitro. The characteristics of the various subpopulations of immune competent cells forming in vitro and in vivo are compared. The capacities and limitations of modeling immunological reactions in a test tube are described.

A model of the in vitro yield of effector cells with delayed type hypersensitivity (DTH) is described. The method involves cultivation of normal splenocytes of mice on a multilayer of adhering syngeneic cells, first processed with antigen. The method makes it possible to distinguish the stage of reprocessing the antigen by auxiliary cells from that of representing the antigen with T-cells and the formation of DTH effectors. It is demonstrated that, given optimal doses of antigen in processing the auxiliary cells, DTH effector cells appear on the second day of cultivation and survive for 6 days. With larger doses of antigens, formation of effector cells is suppressed. L-fucose present in the medium with the antigen, prevents the effects of the migration-inhibiting factor of macrophages on the migrating cells. Monoclonal antibodies to products of I-A and I-E genes suppress the formation and functioning of DTH effector cells. These data attest to the possibility of modeling and regulating DTH reactions in vitro. (2 tables, 4 figures, 35 references.)

G.I. Podoprigora G.I. **Methodological aspects of gnotobiology in biomedical research.** (123)

This paper discusses the problem of obtaining microbe-free animals, and the theoretical aspects of various approaches to its solution. The author proposes a taxonomy of gnotobiological animals based on the ways they were obtained, maintained, and monitored. The use of this taxonomy makes it possible to select the appropriate category of microbe-free animals for experiments. (1 figure; 10 references)

I.G. Sidorovich, V. I. Novikov. **Tissue and functional heterogeneity of cells of mononuclear phagocytic systems.** (13)

The authors analyze data in the literature relevant to heterogeneity, regulatory and effector functions of macrophages and the origins of their subpopulations. They discuss the problem of the development of mononuclear phagocytic systems, their differentiation, distribution among the organs and tissues, and the link between functions and stage of maturation of the cells. They organize the numerous facts concerning the properties of macrophages with suppressor and helper functions and the regulatory reactions of cellular and humoral immunity, and cytotoxic mechanisms of immunological reactivity. Data are presented on the cytotoxic function of the macrophages, which enable make effector reactions of the immune system possible. (2 Figures, 78 references).

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V.Ya. Fel', A. M. Malygin. **Natural killers and the problem of immune surveillance of cytodifferentiation.** (154).

An important role in supporting genetically determined constancy of cellular composition is played by the population of autoaggressive or autoreactive lymphocytes that can recognize antigens of "their own" organism and effect killer reactions with respect to normal mature and embryonic cells that synthesize these antigens. The authors' experimental data showed that in mice a one-time peritoneal immunization with homogenate of normal liver or regenerated liver after a partial hepatectomy, partially simulating disruption of cytodifferentiation, leads to a marked increase in the NK-activity of splenocytes and, at the same time, to increased level of their sensitization to normal hepatic antigens. Judging by the differences in the dynamics natural killer activity and autosensitization it may be hypothesized that these processes, although causally related, are associated with different subpopulations of splenocytes. (1 Figure, 36 references).

R.M. Khaytov, B.V. Pinegin. **B-suppressors: Their properties and functions.** (165).

The authors analyze their own and others' data on the properties and functions of B-suppressors. They demonstrate the existence of B-suppressors in bone marrow and peripheral lymphoid organs, the spleen, and lymph nodes. After immunization with low doses of antigens, suppressor functions of B-cells of peripheral lymphoid organs increase sharply and this capacity is not associated with the mechanism of suppressor activity of specific antibodies. The authors demonstrate the dual mechanism of suppressor activity of immune B-cells. They propose the existence of a single mechanism of B-cell suppression, which monitors and controls the proliferation of immune competent cells, constantly occurring in normal organisms, and also in immunization with low doses of antigen. They conclude that the main role of bone marrow B-suppressors probably involves monitoring and control of colony-forming stem cell proliferation, and also limitation of the proliferation of precursors of antibody producers in the bone marrow. They propose that the T-cell mechanism of suppression is a secondary response triggered in long-term immunization or immunization with supraoptimal doses of antigen. (5 tables, 11 figures, 66 references).

A.N. Cheredeyev, L.V. Koval'chuk, N.K. Gorlina, I.Ya. Stonans IYa. **The participation of the immune system in the processes of differentiation of nonlymphoid tissues: The capacity of lymphocytes to intensify differentiation of transformed fibroblasts in vitro.** (197)

The authors investigated the possibility of the influence of immunocompetent cells on processes of differentiation of nonlymphoid tissues. They used transformed fibroblasts of mice of the transplanted line L (clone 929) as subjects. They evaluated parameters of differentiation of L-cells during joint cultivation with syngeneic cells from the spleens of SZN mice and mononuclear cells of peripheral human blood. The influence of syngeneic and xenogeneic lymphocytes on growth characteristics, morphological and biological criteria was established. Results revealed increased L-cell differentiation. These shifts in the characteristics of L-cells were stable

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and continued for some time during cultivation in the absence of lymphocytes. Lymphocyte supernatants and attached cells had no effect on the differentiation of L-cells. It is proposed that lymphocytes have a differentiating effect on transformed fibroblasts in contact interaction. (4 figures, 39 references)

A.S. Shevelov Unresolved problems with the hypothesis of immune surveillance. (210)

The author discusses certain unresolved aspects of the hypothesis of immune surveillance. He supports the idea that immunological surveillance of tumor growth is a specific case of the surveillance of the immune system of the processes of proliferation and differentiation of cells. The cellular basis of immunological surveillance and the characteristics of this surveillance with respect to tumors induced by retroviruses are considered. (27 references)

G.Z. Shubinskiy. The network theory of immunity and the problem of the integrity of the organism. (221)

The author discusses the significance of N. Jerne's network theory of immunity and the experimental proof for the existence of an immune network from the standpoint of M. Burnett's ideas that immunity is a mechanism for maintaining the integrity of the organism. Based on analysis of data in the literature, the author argues that an immune system organized as a network would have the capacity to regulate morphogenetic processes in the organism, support antigen-structural homeostasis, and foster only coadaptive changes in the quantity of antigen structures of the organism. He discusses the mechanisms of the organization of an integrated immune system, and also the mechanisms through which it would function to support the structural integrity of the organism as a whole.

Yarilin AA. The role of differentiation and modification in the formation of T-lymphocyte heterogeneity. (234)

Heterogeneity of T-lymphocyte phenotype and function occurs on two levels: as a result of the process of differentiation, stable populations of T-cells form, within which, due to cellular environmental factors, variability of traits occurs, which in turn depends on the modifying effects of secondary messengers. The interaction of phenotype and functional variations of T-cells is realized through changes in their "receptor field" and expression of molecules participating in the effector functions of T-cells. (70 references).

LIFE SUPPORT SYSTEMS

PAPER:

P907(20/88) Gitel'son II, Terakov IA, Lisovskiy GM, Kovrov BG, Sid'ko FYa, Okladnikov YuN, Gribovskaya IV, Trubachev IN, Pilenko MI.

Complete regeneration of the atmosphere, water, and vegetable nutrients in a "man -- higher plant" system.

In: Malinin VB, Kosmolinskiy FP, Kuznets YeI (editors).

Perspektivy Razvitiya Kosmicheskoy Biomeditsiny v Svete Iday K.E.

Tsiolkovskiyogo [Prospects for the Development of Space Biomedicine in Light of the Ideas of K.E. Tsiolkovskiy] Proceedings of the XXth and XXIst Lecture Series dedicated to the scientific legacy and development of the ideas of K.E. Tsiolkovskiy., Kaluga 1985, 1988. Section on Problems of Space Medicine and Biology.

Moscow: USSR Academy of Sciences: 1987.

Pages 63-67.

[5 references; none in English]

Authors' Affiliation: Institute of Biophysics, Siberian Division, USSR Academy of Sciences

Life Support Systems, Nutrition

Humans, Man -- Higher Plant System, Botany

Closure, Regeneration

In the Institute of Biophysics of the Siberian Division of the USSR Academy of Sciences, a multiyear project was undertaken involving the creation of a closed ecological system for human life support that would permit bioregeneration of atmosphere and water and recovery of vegetable nutrients.

This paper deals with the latest 5-month experiment with the Bios-3 life support system (LSS) conducted in 1983-1984. As was the case in a previous experiment conducted in 1977, the LSS contained two components: humans and higher plants. The subject "crew" consisted of two individuals.

The experiment's goal was to increase the closure of the LSS:

- 1) With respect to food -- to completely satisfy the crew's requirements for vegetable nutrients.
- 2) With respect to water -- to completely meet all the crew's needs, by having the higher plants utilize the crew's liquid wastes.

The structure of the "higher plants" component and the conditions under which it functioned were altered to increase the quantity of the major vegetable nutrient -- grain and, thus, bread, and to make the diet more varied and nutritionally complete. In addition to the cultures used earlier (wheat, chufa /earth almond/, peas, carrots, radish, beets, onion, dill, cucumber, and potatoes), we added cultures of peas [sic.], tomatoes, and kohlrabi. The higher plant components had to provide the two subjects with virtually all their essential carbohydrates, vegetable protein, fat, and vitamins, in addition to recycling the atmosphere and water.

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The total area occupied by the cultures was 63 m², of which 40 m² was devoted to wheat, 9 m² to chufa, and the remainder to the vegetables.

Wheat was grown in an air subirrigational culture, while chufa and all the vegetable cultures grew hydrophonically on "caramsite".

The improved closure of the water recycling system, compared to that of the previous experiments, was achieved by having human liquid wastes used directly by the wheat culture. The advantage of wheat in this role over other cultures lies in the fact that, first, the edible portion of this culture (grain) is not in contact with the nutritive solution and the liquid wastes added to it. Second, the edible biomass of wheat (up to 60% of the total biomass) acts as a sort of absorber of sodium chloride from the nutrient medium, thus preventing the build-up of sodium and chlorine ions, which are regularly excreted in human urine. The wheat plants received the following percentages (with respect to total intake) of biogenic nutrients from human liquid wastes: nitrogen -- 59%, sulfur -- 28%, potassium -- 19%, phosphorus -- 17%, magnesium -- 13%. The concentration of NaCl in the nutrient solution during the last 45 days remained within the limits of 1-2 g/l. These concentrations are not toxic for wheat and do not interfere with normal growth.

The physical/chemical unit of the BIOS-3 complex included a drying cabinet for plant and food wastes, an apparatus for drying human solid wastes, and a catalytic oven for removing toxic contaminants from the atmosphere. To increase the closure of the LSS with respect to carbon, oxygen, and hydrogen, the unit contained a device for combustion of the nonnutrient biomass of the plants. This device had been altered since the 1977 experiment and produced less nitrogen oxides, which are toxic to plants. Reduction of the nitrogen oxides forming in the combustion chamber with products of incomplete combustion of the biomass took place in the first of the two catalyzers of the thermocatalytic oven.

During the experiment it was established that, due to the shortness of the second catalyzer the contact between the gases and catalyzer was not sufficient for combustion of CO into CO₂. When the volume of the catalyzer was doubled, the atmosphere of the system contained either no CO or quantities not harmful to the crew or plants after combustion of the nonnutrient biomass of the plants.

The presence of CO in the atmosphere during the first period of the experiment decreased the productivity of the plants, but this was corrected by the end of the experiment. There were no effects on the "crew's" health attributable to the brief periods of increased CO in the atmosphere due to thermal reduction of the biomass, since the maximum acceptable concentration was not exceeded. Overall, in this experiment as in the previous ones, a dynamic balance was established between the input and elimination of gaseous toxic contaminants in the system's atmosphere.

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At no time during the experiment was there any sign of illness in the subjects, or even of subjective feelings of diminished well-being. The values of all the measured parameters acting as indicators of the most important physiological functions were rather stable.

The subjects' diet consisted both of products synthesized in the system, and the stores they brought with them. The diet was planned in accordance with the requirements of balanced nutrition and took account of individual tastes.

Plant biomass synthesized in the system met the crew's need for vegetable proteins, lipids, and 95.4% of the carbohydrates. The closure achieved by the system was 70% with respect to dietary calories, 65% with respect to protein, and 35% with respect to lipids.

Consumption of oxygen and elimination of carbon dioxide by the subjects during the experiment was computed as a proportion of the quantity of assimilated (and oxidized) basic nutrients: proteins, fats, and carbohydrates; and the value of the respiratory coefficient was determined to equal 0.867.

Closure of the system with respect to water was 92.1% for this experiment. If the water and nutrient media of the plants had not undergone external analyses, this value, like that of the atmosphere, could have reached the limit of 100%.

The overall evaluation of the system closure was computed using the formula $R = (I - m/M) \cdot 100\%$, where M is the daily requirements of the crew for substances, and m is the daily requirements of the system. The closure coefficient of the cycling of substances in the LSS was computed to equal 91%. The incompleteness of closure is attributed to the introduction of animal products, chemical elements, etc, and removal of liquids for analysis.

MATHEMATICAL MODELING: See Cardiovascular and Respiratory Systems M140

METABOLISM

(See also: Biological Rhythms M142; Body Fluids CR 11)

PAPERS:

P922(20/88)* Savina VP, Mikos KN, Ryzhkova VYe.

The effect of space flights on the concentration of volatile metabolites in the expired gas of cosmonauts.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 47-50; 1988.

[7 references; 2 in English]

Metabolism, Volatile Metabolites, Expired Air
Humans, Cosmonauts
Space Flights

Abstract: This work presents the results of determination of the chemical composition of volatile metabolites in expired gas of cosmonauts before and after space flights varying in duration. Subjects were 20 Salyut-7 cosmonauts, 8 completing long-term flights 3-8 months in duration and 12 completing short-term 7-day flights. Samples of expired gas were collected in soft fluoroplastic containers 2-4 weeks before space flight and during the first hour postflight. Samples were analyzed by chromatography using a flame ionized detector and a column filled with "porapak Q". For purposes of comparison, expired air was analyzed in other subjects after a 120-day period of hypokinesia with head-down tilt followed by 8 minutes of exposure to acceleration to simulate reentry conditions. Expired gas of cosmonauts was found to contain methane, ethane, ethylene, propane, propylene, normal butane, methanol, ethanol, acetone, acetaldehyde, and isopropanol with normal pentane. The majority of these components were elevated after long flights, with greatest increase in aliphatic carbohydrates. Ethane and ethylene, sensitive indicators of lipid peroxidation, increased by a factor of 7. Methane, associated with activity of intestinal bacteria, did not increase in a regular fashion after flight. Alcohols did increase postflight.

Increases in aliphatic carbohydrates and acetone in expired air also occurred after short-term flights, but to a lesser degree than after long-term. After 120-days of hypokinesia with head-down tilt followed by a short period of acceleration, increases in ethane, ethylene, and acetone were as great or greater than after long-term space flight. The authors conclude that space flight, especially long duration space flight, increases lipid peroxidation in humans.

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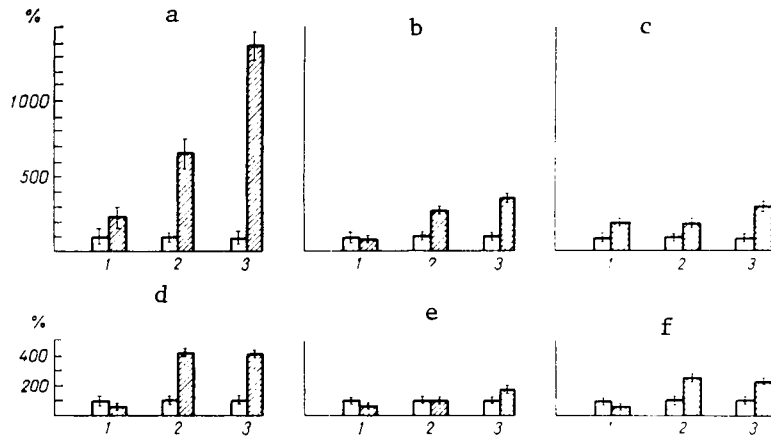


Figure: Changes in concentration (in %) of endogenous substances in expired gas of humans before and after exposure to a set of specific environmental factors

a- ethane and ethylene; b - acetaldehyde; c-acetone; d - methanol; e - isopropanol and N-pentane; f - n-butane; 1 - visiting crew; 2 - prime crew; 3 - hypokinesia with head-down tilt + acceleration; white bars - baseline; hatched bars - after treatment.

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(See also: Adaptation M141; Neurophysiology P940)

PAPERS:

P915(20/88) Buravkova LB, Mailyan ES.

Dehydrogenase activity in skeletal muscles of rats after long-term exposure to weightlessness.

Byulleten' Eksperimental'noy Biologii i Meditsiny.

CV(5): 538-540; 1988.

[11 references; 5 in English]

Authors' Affiliation: Institute of Biomedical Problems, USSR Ministry of Health

Musculoskeletal System, Skeletal Muscles, Dehydrogenases

Rats

Space Flight, Long-Term, COSMOS-1129, Hypokinesia

Abstract: The goal of this research was to study the activity of dehydrogenase of the Krebs cycle, NAD-dependent malate dehydrogenase (MDH) and NADP-dependent isocitrate dehydrogenase (ICDH) in mitochondrial and cytoplasmic fractions, and also lactate dehydrogenase (LDH) in the skeletal muscles (apparently femur, tibia, and quadriceps) of rats that had undergone a 18.5 day space flight on COSMOS-1129 or a 20-day period of hypokinesia. Exact description of subjects and maintenance conditions are not provided, and an earlier publication is referenced. There were 6-10 animals in each group. Enzyme activity was measured spectrophotometrically, and protein activity was assessed using a procedure attributed to Lowry. Multiple t-tests were performed.

On day 1 postflight, activity of the enzymes studied decreased by a factor of 1.5 - 2 compared to the analogous parameter in a control group, suggesting insufficient influx of reduced equivalents from the Krebs cycle into the respiratory chain of the mitochondria. MDH and ICDH activity in cytoplasm was also reduced, but to a lesser extent (50-70%). Judging by lactate, rate of glycolytic processes was lower than in the control group. This phenomenon could be caused either by persistence of response to microgravity, or response to reentry into normal gravity. In a synchronous group in which subjects were exposed to simulations of all space flight factors except weightlessness, MDH and ICDH activity was significantly reduced in mitochondria but to a lesser degree than after space flight. Cytoplasmic MDH, ICDH, and LDH activity showed only a tendency to decrease in this group. This suggests that decrease in enzymatic activity of dehydrogenases after space flight is not a specific reaction of muscle cells to weightlessness, but is a more general response amplified by weightlessness. Six days postflight, mitochondrial MDH and ICDH activity were restored. In cytoplasm, activity of all three enzymes increased by a factor of 1.5 to 2. Analogous parameters in animals in the synchronous condition were no different from those in the control group, suggesting that weightlessness has a specific effect on cytoplasmic dehydrogenases. The authors argue that the immediate postflight effect on the mitochondria attests to a lowered level of functioning, which may be one reason for decreased consumption of oxygen by tissue preparations from the hind limbs of these same rats (described in an earlier publication). Subsequent recovery

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of mitochondrial parameters implies that the effects of weightlessness are reversible. The authors state that increased LDH activity suggests that increased rate of oxidation of the substrate occurs along the glycolytic pathway. The immediate postflight inhibition of cytoplasmic enzymes is considered a response to decreased production of reduced equivalents in the mitochondria. Increased activity 6 days later attests to intensified biosynthetic processes in muscle cells requiring a increased flow of $\text{NAD}\cdot\text{H}$ and $\text{NADP}\cdot\text{H}$ from the mitochondria.

A hypokinesia simulation experiment with rats showed only a tendency for mitochondrial dehydrogenase activity to decrease at the end of a 20-day treatment. In the cytoplasm, ICDH activity decreased reliably on day 10 of treatment, and MDH decreased on day 6 of the recovery period. LDH activity was reduced by half on day 10 of treatment and remained depressed until day 1 of recovery. All parameters were normal after 26 days of readaptation.

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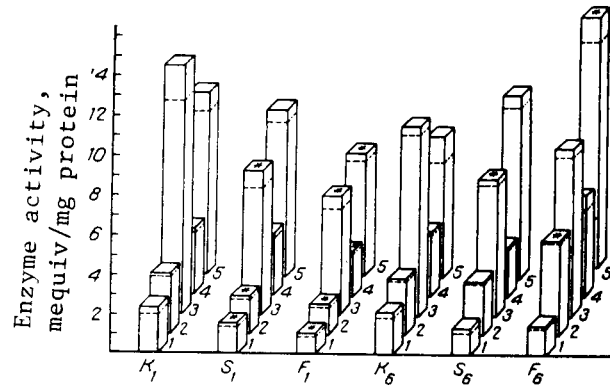


Figure 1: Dehydrogenase activity in the skeletal muscles of rats 1 and 6 days after space flight

Horizontal axis: experimental groups. Dotted line - standard error of the mean. * - significant difference, $p < 0.05$ from the control group. 1 - mitochondrial ICDH; 2 - cytoplasmic ICDH; 3 - mitochondrial MDH; 4 - cytoplasmic MDH; 5 - LDH.

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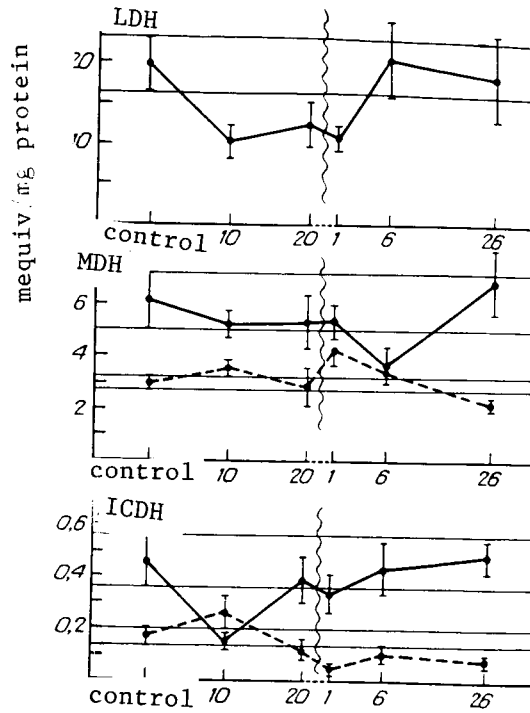


Figure 2: Dehydrogenase activity in skeletal muscle of rats during hypokinesia and subsequent recovery
 Abscissa - day of hypokinesia (10,20) and or readaptation period (1, 6, 26). Solid line - activity of enzyme in cytoplasm; dotted line - activity of enzyme in mitochondria; vertical bars - standard error of the mean for control group.

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P920(20/88)* Khristova LG, Gidikov AA, Aslanova IF, Belyayeva MG, Kirenskaya AB, Kozlova VG, Koslovskaya IB. (Bulgaria, USSR)

The effect of water immersion on motor unit potentials in human muscles.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 39-43; 1988.

[25 references; 19 in English]

Musculoskeletal System, Motor Unit Potentials

Humans

Water Immersion

Abstract: The goal of this study was to increase understanding of the mechanisms underlying the development of changes in muscle fibers in space and during hypokinesia by comparing the potentials of low and high threshold motor units after immersion hypokinesia. Ten individuals underwent "dry" immersion in water at 33.4° C for a period of 3 days. The experimenters studied the extraterritorial potential of motor units of the biceps brachii muscle. The propagation rate and duration of motor unit potentials were recorded using vector electromyography from point surface electrodes. Potentials of low threshold motor units were recorded with two monopolar electrodes located at a distance 10 m along the muscle fibers, less than 20 mm from both the neuromotor synapse and the end of the muscle. To study high-threshold motor unit potentials, a branching electrode placed near the neuromotor synapse was used in addition to the monopolar ones. In three subjects, a high-selectivity conducting electrode was placed under the skin. When a subject achieved a high level of muscle tension on an electromyogram measured from the branching electrode, one high amplitude motor unit was identified, the impulses from which were used to trigger the total EMG recorded by the monopolar electrode. A total of 64 segments of interferent records from the monopolar electrodes were averaged to obtain the high threshold motor unit potential. Each segment included 20 msec before and after the point at which it was triggered. Propagation rate and other parameters were derived analogously for low and high threshold potentials. Rate of propagation was established by measuring time intervals between the negative maxima recorded by the two monopolar electrodes. Total duration of potentials was considered to last from the beginning of the first positive phase to the end of the last positive phase. Since beginning of the first phase was generally not exactly discriminable, it was derived as a function of length of the total depolarized zone. A total of 381 motor unit potentials were recorded, of which 227 were low threshold (74 - control, 75 - day 1 of immersion, 78 - day 3 of immersion) and 154 were high threshold (54 - control, 53 - day 1 of immersion, 47 - day 3 of immersion).

Results indicated that exposure to immersion is accompanied by significant changes in the parameters of low density motor unit potentials. Significant decreases in propagation rate were observed in 9 of 10 subjects. The remaining subject had been repeatedly exposed to immersion and hypokinesia. In the baseline period, mean propagation rate of low threshold potentials was 4.93 ± 0.16 m/sec.; after 1 day of immersion this value was 4.12 ± 0.07 m/sec, and after 3 days - 4.29 ± 0.09 m/sec. Changes were even more striking when the one atypical subject was excluded. Total duration of low threshold potentials increased significantly during immersion, with the value for 1 day of exposure being higher than that for 3 days. Immersion also significantly altered the vector electromyographic pattern (form) of low threshold

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potentials, suggesting shortening of the depolarized zone. Significant changes in parameters of high threshold potentials did not occur. The authors conclude that the main reason for the changes in low threshold motor unit potentials associated with immersion is a sharp decrease in muscle activity. They postulate that the differences in the effects of immersion on high and low threshold motor units are associated with the type of metabolism in the muscle fibers. Oxidative metabolism is characteristic of muscle fibers of low threshold units. One may postulate that immersion facilitated development of a hypoxic process to which low threshold units are sensitive. High threshold motor units, characterized by glycolytic metabolism, are not affected in this way.

Figure 1: Diagram of the multielectrode consisting of two monopolar electrodes (a) and one highly selective branching electrode (b)

Figure 2: Averaged low density motor unit potentials recorded in subject M, before treatment and on days 1 and 3 of immersion

Figure 3: Vector electromyogram image of low density motor units recorded in three subjects before treatment and on days 1 and 3 of immersion

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P923(20/88)* Oganov VS, Skuratova SA, Murashko LM, Guba F, Takach O, Siladi T, Ser A, Rapchak M (USSR, Hungary).

The effect of short-term space flights on physiological properties and composition of myofibrillar proteins of the skeletal muscles of rats.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 50-54; 1988.

[17 references; 4 in English]

Musculoskeletal System, Physiological Properties, Myofibrillar Proteins
Rats, Males, Females, Pregnant
Space Flight, Short-Term, COSMOS-1514, -1667

Abstract: Contraction and composition of contractile proteins of skeletal muscles were studied in rats after a 5-day flight on COSMOS-1514 (pregnant females) and a 7-day flight on COSMOS-1667 (males). On the day of reentry, the animals were sacrificed and muscles from their front (brachial, medial head of the triceps) and hind legs (extensor digitorum longus, soleus, and medial head of the gastrocnemius) were isolated. Contractile properties were studied in preparations of glycerinized muscle fibers in a solution of ATP+Ca²⁺. Absolute and relative concentrations of nitrogen proteins were determined in samples of muscle tissue frozen in liquid nitrogen. Cellular fractions of proteins (myofibrillar and sarcoplasmic) were prepared and analyzed. The quantitative relationships among fractions of myofibrillar proteins was determined using electrophoresis on an SDS-polyacrylamide gel. Results for flight animals were compared with those for a synchronous control and a vivarium group.

In rats of both flight groups, there was a reliable decrease in wet weight of all muscles studied. Loss of mass in muscles involved in postural activity (triceps and soleus) increased progressively from the 5- to the 7-day flight. Loss of mass in the fast-twitch muscles was somewhat greater after the 5-day flight. All muscles studied showed decreased force of contraction after the 5-day flight, but this effect was less pronounced in the medial head of the triceps; however, loss of strength in the fibers of the brachial and gastrocnemius muscles was as pronounced in synchronous controls as in flight animals, and loss was more pronounced in the latter group in the extensor digitorum longus. Decrease in force of contraction was noted only in the soleus in the flight groups. After the 7-day flight, contractile force was significantly lower in the postural muscles of the hind legs in flight animals than in other groups, but was virtually unchanged in the postural triceps and fast-twitch extensor digitorum longus, and showed a tendency to increase in the brachial muscle. Rate of contraction after the 5-day flight was decreased in all muscles except the extensor digitorum longus. After the 7-day flight, rate of contraction was significantly decreased in the fast-twitch brachial and slow soleus muscles but did not undergo significant changes in the remaining muscles studied. After this same flight, rate of semirelaxation of muscle preparations was decreased in the extensor digitorum longus, medial head of the triceps, and soleus muscles, and unchanged in the remaining ones.

Effects of weightlessness on composition of contractile proteins were more marked in the soleus, triceps, and gastrocnemius muscles. After the 5-day flight, the number of "slow" light chains of myosin in the medial head of the triceps increased by approximately a factor of 4, while the "fast" myosins decreased by 50%. Amount of slow myosin chains was unchanged in the

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gastrocnemius and soleus, while fast myosin chains decreased in the soleus and increased in the medial gastrocnemius. The ratio of fast to slow light chains of myosins decreased by approximately 35% in the soleus and medial head of the triceps and increased by 90% in the medial gastrocnemius. After the 7-day flight, this ratio increased by 50% in the soleus and gastrocnemius, and decreased by 60% in the triceps.

The authors conclude that the reactions of skeletal muscles of rats during the initial period of weightlessness mainly reflect changes at the level of regulation, which do not lead to the restructuring of the functional profile of muscles observed after more prolonged flight. These changes are not as pronounced after short-term flights, partially due to limitations on their development because of the relatively low rate of metabolism of contractile proteins in the muscles.

Table 1: Muscle mass (in mg) in rats after short-term space flights

Muscle	Flight Duration, days	Flight	Group Vivarium	Synchronous
Brachial	5	162.0*,+	194.6	203.4
	7	173.5	205.7	208.3
Medial head of triceps	5	126.6*,+	161.6	170.6
	7	111.3*,+	171.3	167.3
Extensor digitorum longus	5	118.0+	129.8	142.6
	7	146.7*,+	168.0	174.6
Soleus	5	108.8+	123.2	131.6
	7	122.4*,+	163.7	172.4
Medial gastrocnemius	5	494.6*	596.0	583.5
	7	671.4*,+	801.7	752.9

Here and in tables 2 and 3; + - differs significantly from synchronous group; * differs significantly from vivarium group ($P < 0.05$).

Table 2: Force of contraction (in $\text{N} \cdot \text{mm}^{-2} \cdot 10^{-1}$) muscle fibers of rats after short-term flights

Muscle	Flight Duration, days	Flight	Group Vivarium	Synchronous
Brachial	5	1.28*,+	2.66	1.66*
	7	4.83+	4.46	3.88*
Medial head of triceps	5	2.37	2.83	2.81
	7	5.35	5.41	5.51
Extensor digitorum longus	5	2.02*,+	2.56	1.82*
	7	6.65	6.71	6.59
Soleus	5	3.16*,+	6.27	5.48
	7	4.55*,+	8.20	7.95
Medial gastrocnemius	5	1.74*	2.51	1.95*
	7	2.71*,+	3.96	3.88

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Table 3: Maximal rate of development (in $\text{g}\cdot\text{sec}^{-1} 10^{-3}$) isometric contraction of preparations of muscle fibers of rats after short-term space flights

Muscle	Flight Duration, days	Flight	Group Vivarium	Synchronous
Brachial	5	24.25*,+	43.36	32.19*
	7	42.29*,+	56.50	49.80
Medial head of triceps	5	20.60*,+	29.55	28.56
	7	50.47	45.72	50.74
Extensor digitorum longus	5	36.83	34.62	34.38
	7	52.06	53.40	46.69
Soleus	5	21.35*,+	41.26	38.64
	7	21.80*,+	30.12	28.14
Medial gastrocnemius	5	26.36*,+	32.48	35.92
	7	54.04	54.90	47.55

MUSCULOSKELETAL SYSTEM

P925(20/88)* Burkovskaya TYe, Vorozhtsova SV.

The effect of hypokinesia on the osteogenic and hemopoietic function of bone marrow in mice: Studied in ectopic bone.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 61-65; 1988.

[15 references; 2 in English]

Musculoskeletal System, Hematology, Bone Marrow, Osteogenic and Hemopoietic Functions, Ectopic Bone

Mice

Hypokinesia

Abstract: Experiments were conducted on SVA male mice and (SVA X S57Bl)F₁ hybrids. These subjects received implants below their renal capsule of 1/2 of a bone marrow cylinder from the femur bone of the donor. The number of cells in the implanted fragments varied from $(0.8 \text{ to } 1.7) \cdot 10^7$ with a mean of $1.3 \pm 0.01 \cdot 10^7$ cells. On day 30-35 after implantation, the newly formed bone marrow organ was removed and weighed, and smears were prepared for determining its cytological composition. The remainder of the bone marrow was flushed and the ectopic bone dried and weighed. Two experiments were run. In the first, bone marrow donors were subjected to hypokinesia (induced using immobilization cages) while recipients were maintained under normal conditions before and after implantation. In experiment 2, recipients underwent a 3-week period of hypokinesia, with the implantation 5-7 days before this treatment. In this experiment donors were treated normally. The 2 experiments together utilized 260 recipients and 200 donors.

Animals exposed to hypokinesia showed marked behavioral and physiological signs of stress. Bone marrow from donor mice in the period of the most severe stage of hypokinetic stress (3-day exposure) and the period of relative adaptation (3-week exposure) developed ectopic bone indistinguishable from that formed when donors were maintained under normal conditions. This suggests that the quantity of osteogenic precursors and their functional activity are unaltered by a 3-week period of hypokinesia. Number of myelokaryocytes in the implant did not differ when donor was exposed to hypokinesia. The ectopic hemopoietic focus also did not appear to be affected by immobilization of donors. In the second experiment, where marrow from intact donors was implanted in mice subsequently exposed to 3 weeks of hypokinesia, intact osteogenic precursor cells and hemopoietic stroma formed a normal osteoid and hemopoietic microenvironment. However, after 3 weeks of hypokinesia, the newly formed organ was significantly (by approximately 40%) below the control group in the weight of bone and hemopoietic tissues. When the cellular composition of the implant was examined in intact recipients after a month, it was found that the hemopoietic focus was still being formed. This tissue differed from that of the femur bones in lower concentration of granulocytes and higher numbers of erythroids and lymph-like cells. This difference was also found when recipients were exposed to hypokinesia.

The authors conclude that hypokinesia depresses the development of ectopic bone and foci of ectopic hemopoiesis in heterotropic transplantation of syngenic bone marrow below the renal capsule of mice. The data obtained suggest that the leading factor in inhibition of the processes of ectopic osteogenesis when mice are exposed to hypokinesia is the acute stress reaction accompanied by increased production and secretion of

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glucocorticoids. It can be assumed that the processes of inhibition of osteogenesis also apply to the osteogenic component continuously remodeling the skeletal bones. Thus, the stress effects of long-term restricted movement makes a definite contribution to the development of systemic osteoporosis as a result of inhibition of neogenesis of bone tissue. The most sensitive stage of osteogenesis is the period of formation of the organic portion of the bone matrix, when the osteoblasts (target cells for the effects of glucocorticoids) actively synthesize bone proteins. However, it is clear that osteogenic precursor cells and stromal precursors that create the hemopoietic microenvironment retain their functional activity even during hypokinesia.

Table 1: Weight of stress-sensitive organs, ectopic bone and ectopic hemopoietic focus

Group	Weight				
	body, g	spleen, mg	thymus, mg	ectopic bone, mg	ectopic hemopoietic focus, mg
1	24.8 (110)	88.6 (77)	38.2 (95)	1.28 (120)	5.69 (91)
2	18.6 (51)	42.2* (51)	9.6* (51)	--	--
3	24.8 (56)	88.6 (35)	39.1 (56)	1.26 (74)	5.71 (65)
4	26.7 (32)	81.3 (24)	41.1 (24)	1.20 (31)	5.58 (24)
5	16.8 (37)	44.1 (37)	15.7* (37)	0.75* (37)	3.22* (37)

Group 1 - intact donor - intact recipient; 2 - 3-day hypokinesia; 3 - 3-day hypokinesia, donor - intact recipient; 4 - 3-week hypokinesia, donor - intact recipient; 5 - intact donor - 3-week hypokinesia, recipient. * - difference from group 1 statistically significant ($p < 0.001$). Numbers in parentheses indicate number of animals.

Table 2: Cytological composition of bone marrow in femur and ectopic bones

Bone	Hemopoietic cells, %		
	Granulocytes	Erythroid elements	Lymphocytes
Tibia			
Control (N=21)	56.5	19.4	23.3
3-week hypokinesia (27)	60.0	19.5	19.1
Ectopic bones			
Control (17)	44.6*	23.5*	29.8*
3-week hypokinesia	48.1*	24.0*	25.6*

* - differences between femur and ectopic bone statistically significant.

MUSCULOSKELETAL SYSTEM

P926(20/88)* Shvets VN, Pankova AS, Kabitskaya OYe.

Prevention of osteoporosis by injecting rats with xydifon before or during hypokinesia.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 65-70; 1988.

[13 references; 9 in English]

Musculoskeletal System, Osteoporosis, Prevention

Rats

Hypokinesia, Pharmacological Countermeasures, Xydifon

Abstract: It was previously shown that high doses of xydifon (or ksidadifon: hydroxyethylidene biphosphonic acid) inhibit the resorption and metabolism of bone tissue that accompanies increased bone mass in normal animals. This study investigated the effectiveness of this drug in preventing disuse osteoporosis in rats exposed to hypokinesia. Male Wistar rats were divided into seven treatment groups. Group 1 was the control; group 2 spent 32 days under conditions of "pure" hypokinesia (model not specified); group 3 was injected subcutaneously with 10 mg/kg xydifon for 7 days and then sacrificed and studied; group 4 received the identical drug treatment for 7 days and was maintained for the subsequent 32 days under normal laboratory conditions, after which the rats were sacrificed and studied; group 5 received xydifon for 7 days and then spent 32 days in hypokinetic conditions; group 6 and 7 animals were treated identically to those in group 5, except that during the hypokinesia period they were injected daily with 1 and 5 mg/kg of xydifon, respectively. Each group contained 10 subjects. After treatment, subjects were sacrificed and their tibia, femur, brachial, and vertebrae (at the level of the lumbar area), sterna, and iliac bones isolated. Tissue was fixed (solution of 5% formaldehyde) with Muller's fixative and decalcified in 7% trichloroacetic acid and poured into histoplast. Longitudinal cross sections 5-7 um thick were prepared through the center of the long bones (proximal end of the tibia and brachia and distal end of the femur) and bodies of the vertebrae, sterna and iliac bones and stained with hematoxylin, eosin, or toluidine blue. The state of bone tissue was evaluated histomorphometrically for the following parameters: three-dimensional density of total spongy bone in the area of the primary spongiosa of the tibia, vertebrae and sternum 0.5 mm from the lower edge of the epiphysial growth layer, and width of the epiphysial growth layer and its individual cartilaginous zones. Three-dimensional parameters were determined using an ocular matrix. The number of osteoblasts and osteoclasts in a visual field (mag. 400 X) were counted in the zone of the primary spongiosa of the bones of the legs and trunk. Statistical testing utilized Student's t.

A period of 32 days of hypokinesia reduced the density of all spongy bone by more than 50% in the metaphysis of long bone and by approximately 15% in the bones of the trunk and pelvis compared to the normally treated controls. Injection of 10 mg/kg xydifon for 7 days increased the mass of spongy bone in the leg bones of otherwise normally treated rats to 120% of baseline immediately after treatment. This parameter was unchanged in other bones. When the effect of xydifon was measured 32 days after treatment termination (group 4), spongy bone density did not differ from baseline in any bones studied. When 7 days of xydifon was followed by 32 days of hypokinesia, no bone loss was noted in any bone after the combined treatment. Administration of xydifon during and prior to hypokinesia significantly

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increased spongy bone density in long bones relative to intact controls significantly. Other bones were not significantly affected. The higher dose of the drug (5 mg/kg) (group 7) was associated with a greater increase (up to 150% higher than for control subjects).

Histological examination showed that hypokinesia decreased density in the metaphysis of long bones. In this group, width of the epiphyseal growth layer decreased by 30-40%, with the width of the hypertrophic and proliferation zones also narrowing. In groups 4-6 bone density did not decrease in the secondary spongiosa; however, between the primary and secondary spongiosa were "pockets" varying in width and devoid of bone tissue, i.e. the majority of spongy bone moved away from the primary spongiosa in the direction of the diaphysis. In these groups the growth layer was identical in width to that of animals in group 2 (hypokinesia alone). In group 7, spongy bone grew denser, forming a continuous "fence". Width of the epiphyseal growth layer increased in this group due to increases in the hypertrophic zone and exceeded baseline level. These changes did not occur in the trunk and pelvis bones.

When density of the primary spongiosa was measured it was found that mass of spongy bone in the tibia of rats in groups 4 and 5 had decreased significantly compared to baseline. Additional xydifon in dose of 1 mg/kg during hypokinesia did not correct this problem, while a dose of 5 mg/kg increased density to 160% control level. Similar but less pronounced results occurred in the bones of the trunk. Similar losses of bone tissue in primary spongiosa in groups 4 and 5 suggest that these changes are not due to hypokinesia but to preliminary administration of xydifon, which inhibited longitudinal bone growth. This is corroborated by the fact that width of the epiphyseal growth layer was the same in these two groups. The increase in bone mass throughout the metaphysis and in the primary spongiosa area can be explained by inhibition of the calcification zone of the epiphyseal growth layer. The hypertrophic zone of cartilage broadens due to longitudinal bone growth.

Hypokinesia led to proportional decreases in osteoblasts and osteoclasts in tibia and trunk bones. Injection of xydifon (not accompanied by hypokinesia) led only to decrease in number of osteoclasts in both types of bone, with osteoblasts virtually unaffected. The decrease in osteoclasts in the trunk were seen in all cases where xydifon was used. In the tibia, changes in osteoclasts depended on specific conditions. Rats in groups 4 and 6 showed increase in osteoclasts in this bone, but not to control level. In animals of groups 5 and 7, osteoclasts decreased in the tibia. Osteoblasts in the tibia of animals in groups 4-7 decreased compared to those of animals in groups 1-3. The authors conclude that xydifon increases the involvement of precursors to osteoblasts in formation of new bone. The effectiveness of xydifon (administered before and/or during hypokinesia) in preventing osteoporosis makes this a promising drug for use in space medicine.

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Table: Number of bone cells per 1% bone mass, in the area of the primary spongiosa of various bones

Group	Tibia bone		Bones of the trunk	
	Osteoblasts	Osteoclasts	Osteoblasts	Osteoclasts
1	2.0	0.38	0.67	0.23
2	1.2	0.22	0.37	0.10
3	1.3	0.13	0.67	0.11
4	0.7	0.46	0.06	0.16
5	0.15	0.33	0.08	0.15
6	0.37	0.70	0.10	0.18
7	0.24	0.08	0.19	0.09

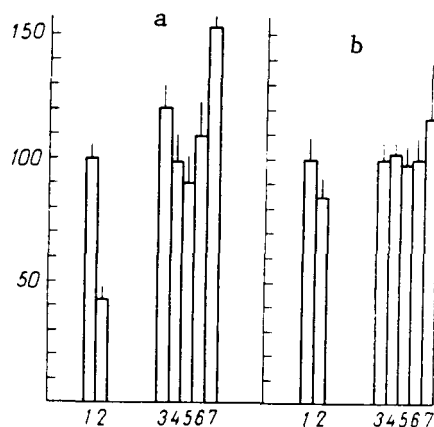


Figure 1: Histogram of three-dimensional density of total spongy bone in the metaphysis of long bones (a) and bones of the trunk and pelvis (b)

Here and in Figure 3: abscissa - group; ordinate - bone density (in % of normal control, taken as 100%). Vertical lines - confidence interval for $p=0.05$.

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Figure 2: Microphotographs of the metaphysis of long bones of rats
a - e -- animals in groups 1, 2, 5 - 7, respectively. 1- bony edge of
the epiphysial center of ossification; 2 - epiphysial growth layer; 3 -
primary spongiosa (bone); 4 - transitional zone; 5 - secondary spongiosa.
Hematoxylin and eosin.

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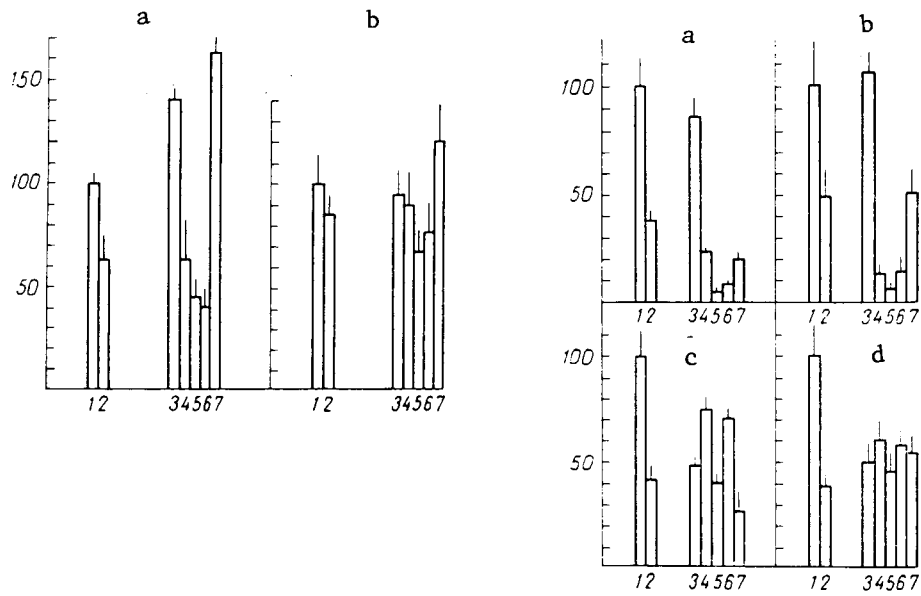


Figure 3: Histogram of three-dimensional density of spongy bone in the area of the primary spongiosa of the tibia (a) and in the bones of the trunk (b)

Figure 4: Histogram of the quantity of osteoblasts (a) and osteoclasts (b) in the tibia (c) and bones of the trunk (d)

Abscissa: group; ordinate: number of cells (in % of intact control)

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P935(20/88)* Volozhin AI, Stupakov GP, Kazeykin VS.

Hypogravity-induced changes in bones.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 4-13; 1988.

[79 references; 45 in English]

Musculoskeletal System, Bone Changes, Mineralization, Strength
Humans and Animals
Microgravity, Space Flight

Abstract: This paper reviews the literature on the effects of weightlessness on bones. The authors conclude that in order to understand the major changes in the strength characteristics of bones occurring in response to altered gravity, it is sufficient to study two parameters: the concentration of mineral substance in spongy bone and the mineralization of the organic matrix. Of these, the latter is more important and, furthermore, can be measured noninvasively using computer tomography. Data in the literature support the conclusion that space flight inhibits all aspects of bone growth. Bones bearing the body's weight under normal g are most affected by microgravity, and the spongy structures are more altered than compact ones. Comparative interspecies studies show that magnitude of osteodystrophic changes is positively associated with metabolic rate and negatively associated with the initial density of bone structures. Space-flight-induced osteodystrophic changes include decrease in bone mass, small decreases in degree of mineralization of existing bone structures, and some decrease in Ca in their mineral component. There is a dissociation within the bone mineralization process with low mineralization of the organic matrix forming in hypogravity accompanying hypermineralization of old structures. These changes are caused by inhibition of osteogenesis and unchanged or increased rate of resorption.

Before clear symptoms of decreased bone mass occur in space, certain species show small decreases in Ca in the mineral component and marked decreases in strength of compact or spongy bone. The authors explain these changes as follows: absence of gravitational loading in weightlessness induces weakening of the functional and hydroxyl associations between the organic and mineral components, decreasing the rigidity of bone and "equalizing" the tension. The mechanism underlying these changes may be loss of ions from the surface of the crystal. Since this layer contains only calcium, and not phosphorus ions, the decrease in calcium in the mineral component is explained. Changes in the collagen-crystal associations also explain decrease in the mechanical properties of bone, in turn explaining that after weightlessness or its analogues, spongy bone retains its normal association between strength and density, while compact bone exposed to hypokinesia is weaker for a given density than normal compact bone. Although bone starts to regain its density after space flight, evidently the stress of readaptation further weakens collagen-crystal bonds. Thus, on day 6 postflight, bones of rats flown on COSMOS-1129 showed further decrease in concentration of calcium in the mineral component, accompanied by decrease in bone strength despite increased density.

The authors hypothesize that the trigger for osteodystrophy in response to microgravity is decreased generation of electric potentials. This evidently acts as a direct stimulus for the migration of T-lymphocytes from the blood into the bone tissue, where, activated by monocytes through emission of PGE,

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they begin to produce osteoclast-activating factor, which has been shown to inhibit osteogenesis, possibly by inhibiting synthesis of BMP (bone morphogenetic protein), as reflected in retardation of the maturing of new structures. OAF also increases the population and activity of osteoclasts, sharply increasing resorption, but data on whether this occurs in space are contradictory. (Perhaps, when gravity loading is removed, it is not osteoclast resorption that increases, but another perlacunary resorption pathway.) In addition, regulation by osteotrophic vitamins, hormones, and prostaglandins are hypothesized to play a role in the effects of space flight on bone. Vitamin D is thought to be particularly important. Changes in blood supply to bones in microgravity may also be important.

The authors conclude that bone changes in space result from processes under complex multi-level regulation. A detailed study of all components of this process may provide important contributions to many areas of space and clinical medicine.

Figure : Interaction between mechanical and morphological characteristics of spongy and compact bone

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P944(20/88) Oganov VS.

Neurotrophic influences in the adaptation of skeletal muscles and motor functions to weightlessness.

In Nasledov GA (editor).

Mekhanizmy neyronal'noy regulyatsii myshechnoy funktsii [**Mechanisms of neuronal regulation of muscle function.**]

Leningrad: Nauka; 107-137; 1988

Author's Affiliation: Institute of Biomedical Problems; USSR Ministry of Health

Musculoskeletal System, Skeletal Muscles, Fast- and Slow-Twitch, Motor Function, Neurophysiology, Neurological Control, Adaptation, Protein Turnover

Rats, Dogs, Humans

Space Flight, Short-Term, Soyuz-9, COSMOS-605, -690, -936, -1129, Immobilization, Hypokinesia, Hypodynamia, Tail-Suspension, Amputation, Motor Patterns

Abstract: This chapter summarizes and draws conclusions from the results of three groups of experiments. Analysis is guided by the general goal of determining how neurotrophic factors integrate adaptive changes in muscle during space flight (particularly the effects of weightlessness and the consequences of these changes for motor function after return to Earth).

One viewpoint postulates that the motor disturbances noted during the first days of exposure to weightlessness are associated with changes in various inputs to the motor control system. This system, which through evolution has adapted to a certain level of gravity, could not function without constant flow of afferent proprioceptive feedback to guide adjustment of motor programs. Changes in skeletal muscles per se are observed after longer term exposure to weightlessness. The first muscular effects appear soon after abatement or disappearance of the initial motor disturbances during the acute period of adaptation to weightlessness, or on Earth after completion of short-term (up to 3 weeks) flights.

These tendencies were most pronounced on an 18-day flight on Soyuz-9, throughout which prophylactic measures were used less extensively than during subsequent flights. Certain problems observed at the beginning of the flight with cosmonauts' estimations of muscle force and use of forces inappropriate to particular motor tasks were overcome by days 3-4 of the flight, attesting to the development of a new motor template providing motor coordination appropriate to the new conditions. However, the physical work capacity of the cosmonauts decreased noticeably after 12-13 days of flight, as reflected in fatigue occurring at the end of each day during the last third of the flight. Postflight, the members of the Soyuz-9 crew displayed a significant loss in muscle mass and strength of the lower limbs, and marked postural and motor disruptions. Other long-term flights have been associated with similar changes.

These results are consistent with differences between the motor regulating system and the skeletal muscles per se in rate of adaptation to weightlessness. Current theories postulate that ongoing control of movement and posture (a special case of movement) is a major function of the central nervous system. Without considering neural (efferent) activation of muscles with neurotransmitters, there are several ways motoneurons can influence

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muscles: neurotrophic substances such as morphogens that are released by nerve impulses, neurohormones, or other humoral effects. Neurotrophic factors require substantially greater time (hours and days) to take effect. The main function of such factors is to support the skeletal muscles in a differentiated state. Each muscles will have a particular distribution of the different motor fibers in accordance with its primary function.

A major presupposition of the author's research is that at least two regulatory systems, differing in time constants, participate in the genesis of gravity-dependent changes in motor functions and the state of skeletal muscles (particularly during space flight). In accordance with this idea, the first group of experiments involved study of the contractile characteristics of muscle fibers and preparations of isolated muscles in white rats after flights of approximately 3 weeks, on the COSMOS biosatellites.

COSMOS Space Flight Results

Motor activity was recorded during flight and the properties of isolated muscles of the hind limbs - the soleus and extensor digitorum longus -- were studied postflight. Parameters of isometric contraction (force, speed of contraction, fatigability) of prepared muscles were recorded while delivering unitary and rhythmic stimulation (smooth tetanus) (COSMOS-605, -690). For some flights (COSMOS-936, -1129), muscles of the forelimbs, the medial head of the triceps, and brachial muscles, were also investigated by measuring amplitude-time characteristics of their isometric contractions in a solution of ATP + Ca^{2+} . Strength and speed of contraction were computed. Impulse force, was used as a measure of work capacity. Synchronous and vivarium control groups were used.

[Absolute] Loss of muscle mass occurred in the order brachial muscle < extensor digitorum longus < medial head of the triceps < soleus muscle. The greatest [relative] loss in mass was noted in the soleus (56%), and the least in the extensor digitorum longus and brachial muscles (10 and 16%, respectively). Preparations of isolated soleus muscles demonstrated a significant decrease in maximum amplitude of smooth tetanus (A_T , by 30-68%) and in absolute strength (A_T per unit mass - by 21-35%). In preparations of the extensor digitorum longus, the changes in these parameters showed similar tendencies in both the flight and synchronous groups. No changes were noted in the amplitude of a single response (A_0) in either muscle. There was a decrease (by 20-58%) in the magnitude of the ratio A_T/A_0 in the soleus muscle.

Immediately postflight the soleus alone displayed statistically reliable changes, including decrease in resistance to fatigue, increase in rigidity of the muscle during passive extension to 1.3 times its length at rest, "acceleration" of the contraction process, and decrease (by 26-48%) of the time for tetanus to develop to half of A_T . These parameters, except for strength, recovered by day 26 postflight.

The capacity of muscle fibers to develop force after space flight was also decreased significantly (by 36-48%) in preparations of the soleus and medial head of the triceps. These muscles displayed the greatest loss of mass and a

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statistically significant decrease in fiber diameters. In contrast, the contractile strength of fast-twitch fibers either changed only slightly (extensor digitorum longus, COSMOS-1129), or increased to a statistically significant extent (brachial muscle, COSMOS-946). Work capacity of single fibers in the soleus and medial head of the triceps was depressed after space flight, and was close to the work capacity of fast-twitch muscle fibers. The latter was for the most part virtually unchanged, but in one case (brachial muscle, COSMOS-936) exceeded control values. In this same instance there was an increase in the mean diameter of brachial muscle fibers.

Postflight contraction speed of muscle fibers after space flight increased in the soleus and either only slightly altered or tended to decrease in preparations of the medial head of the triceps (COSMOS-1129). Artificial gravity corrected or attenuated changes in physiological properties of the medial head of the triceps and brachial muscles (COSMOS-936).

Based on decrease in contraction speed in the norm the muscles studied can be placed in the following order: brachial < extensor digitorum longus < medial head of the triceps < soleus muscle. Changes in functional characteristics of muscles in the flight and control groups suggests that changes in the postural muscles (soleus, medial head of the triceps) were directly caused by gravity. In contrast, changes in temporal characteristics of fast-twitch muscle (brachial muscle and extensor digitorum longus) functions were similar in flight animals to those occurring in the synchronous control conditions. Analysis of these results suggests that these are most likely caused by the totality of flight factors including the maintenance conditions of the animals. In particular, hyperfunction in the brachial muscle may be explained by behavioral adaptation of the animals to weightlessness, because when the animal attempts to stabilize its body position, it mainly increases activity (including tonic activity) of its forelimbs, which in the rat are better adapted to highly differentiated movements. This circumstance is associated with a statistically reliable increase in the total motor activity of the animals in flight, as noted in biosatellite experiments.

The changes observed in the morphofunctional characteristics of muscles, which are most pronounced in the soleus muscle (decrease in muscle mass and fiber dimensions, decrease in strength capacities, loss of elasticity) agree well with results of other morphological and biochemical analyses performed on analogous material in biosatellite experiments. Such changes attest to the development of pronounced atrophy and stimulation of albuminolysis in the soleus muscle. In the extensor digitorum longus and other fast-twitch and mixed muscles of the hind limbs, no such changes were observed. Nor were there changes in the contractile properties of glycerinated motor fibers.

The cited results of physiological research also support the hypothesis that the postural muscles, especially the soleus, undergo adaptive changes in addition to atrophy and hypodynamia. These effects can be observed in the acceleration of contraction time in single muscle fibers and isolated soleus muscles. This is further corroborated by the decrease in the ratio between the amplitudes of tetanic and single responses ($A_T:A_O$) in the isolated

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soleus, which is indicative of the changes in the proportions of slow- and fast-twitch fibers, increasing the number of the latter. This hypothesis is confirmed by the results from morphological and biochemical studies in biosatellite experiments. Data were obtained on the isoenzyme spectrum of myosin and the fractional composition of troponin-tropomyosin complex, which changes in a manner analogous to changes in contractile speed in the muscles of the same animals. The distinct increase in myosin with a LTs-3 light chain in the soleus deserves special attention. In the norm, the soleus contains only traces of this fragment of the myosin molecule. This component of "fast myosin" is associated with high ATPase activity of the fast-twitch muscle fibers. At the same time, fast muscles showed evidence of restructuring of the myosin populations, with an increase in the isoforms of "slow" myosins.

Histochemically, flight animals displayed a sharp decrease in oxidative enzyme activity in the red fibers of the soleus muscle. Changes in the lactate dehydrogenase isoenzyme spectrum were also observed, confirming that aerobic respiration was inhibited and glycolytic metabolic pathways were activated.

The author concludes that the data suggest that rat skeletal muscles react to weightlessness or the entire set of space flight factors as a system. The magnitude and direction of changes in a particular muscle depend on the extent of its involvement in postural activity (in a given species of animal) and also on the anatomical/topographical and biomechanical characteristics of the muscle.

When changes in the contractile properties of antigravity muscles -- the slow-twitch soleus and fast-twitch medial head of the triceps -- are compared to those occurring in the fast-twitch flexor muscles -- the brachial and extensor digitorum longus -- the hypothesis that they adapt differently to space flight is supported. Two types of active adaptation can be distinguished in the antigravity muscles. One of these is manifest in reversible disuse atrophy and loss of strength and, evidently, decrease in elasticity, which may be the consequence of a partial replacement of the functional proteins by stromal proteins. The second type of adaptation is involves the restructuring of myosin populations in the fibers of postural muscles resulting in an increase in their contraction speed. Evidence for these two types of adaptation is especially clear in the soleus muscle.

The fast-twitch flexor muscles display virtually no signs of the first reaction type. Adaptive processes of the second type are either very weakly manifested or lead to muscle hypertrophy accompanied by a slowing of contraction, which is most pronounced in the brachial muscle.

The different reactions between the postural and fast-twitch flexor muscles to space flight conditions are probably caused by more than their differing functions, since their activity changes in different ways under these conditions. Judging by the results cited above, only changes in antigravity muscles are associated directly with weightlessness. Reactions of the fast-twitch flexor muscles are determined more indirectly.

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Ground-Based Models

In the second group of studies, the significance of various components of movement for maintaining muscles in the normal (differentiated) state was assessed. In one experimental condition the predominantly phasic component of movement was excluded (hypokinesia); in a separate condition, the tonic component and the support loading on the muscles were eliminated (hypodynamia). Hypokinesia was produced by housing animals in immobilization cages. Hypodynamia was created in the muscles of the forelimb by amputating the distal portion of the leg and in the muscles of the hind limbs, by suspending the animals [by the tail] in special cages where they could move around using only their forelimbs. In addition, activation of the postural muscles by long-term (22 days) exposure to centrifugal acceleration was studied.

Preparations of isolated muscles were used to study the effects of long-term hypokinesia (30-120 days), hypodynamia in the amputation model (up to 3 months), and the effects of $+2G_x$ acceleration. The contractile properties of the muscle fibers were studied after hypokinesia, hypodynamia ("tail suspension" model), or exposure to acceleration, all lasting 22 days. The same muscles and contraction parameters were studied as those in the biosatellite experiments, with the exception of long-term hypokinesia, where only the contractile properties of isolated plantaris muscles were studied.

Neither intact muscles nor muscle fibers showed any appreciable signs of the development of atrophy in the postural muscles after 22 and 30 days of restricted mobility. Only after more prolonged hypokinesia were there indications of decreased amplitude of a single contraction and tetanic contractions in the soleus (after 90 days) and extensor digitorum longus (after 120 days), and decreased resistance to fatigue in the soleus (preparation of isolated muscle, 120 days). However, during this period no changes were noted in absolute strength (A_T per unit mass) in the muscles studied. Changes included selective slowing of isometric contractions in preparations of the soleus and plantaris after 90 and 120 days of experimental treatment; increase in time to develop tetanus (to half of the maximum) by 51 and 21%, respectively; and increase in half-relaxation time, by 31 and 43%, respectively.

The "unloading" of the shoulder muscle in rats due to amputation of the distal third of the forelimb ("amputation" model of hypodynamia) was accompanied by statistically reliable decreases in the mass of the medial head of the triceps. Mass of the flexor brachial muscle in the operated leg on did not change. The medial head of the triceps muscle also displayed a decrease in absolute strength. No effects were seen in the strength characteristics of the brachial muscle. The contralateral leg, on the other hand, showed a statistically significant decrease in the amplitude of tetanus and absolute strength of the brachial muscle.

Contraction time in the medial head of the triceps in the amputated leg accelerated; the time to achieve half-maximum relaxation after a tetanic contraction decreased; and "functional mobility" increased. On the other hand, a statistically reliable "slowing" was noted in contractions of preparations of the brachial muscle both in the amputated and, to a more

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pronounced extent, the contralateral leg. Both legs exhibited a decrease in the contraction rate in smooth tetanus.

The contractile properties of glycerinized muscle fibers confirmed that their reaction to unloading ("tail suspension" model, 22 days) was also highly selective and dependent on the functional profile of the fibers. A statistically significant loss of muscle was noted only in the soleus and medial head of the triceps. The soleus also showed a more significant decrease in the mean diameter of fibers. All the muscles studied showed a decrease in the strength of isometric contraction of fibers which was statistically reliable in the soleus and medial head of the triceps. The soleus exhibited a weak tendency toward a faster contraction.

Thus, this research attests to qualitatively different trends in the physiological responses to hypokinesia (maintenance in cramped cages) and hypodynamia (elimination of loading on the muscle by amputation or tail suspension) in the postural skeletal muscles of rats. The hypodynamia model affects the postural muscles in a manner phenomenologically identical to the effects of weightlessness on those same muscles. These functional changes observed in the unharmed postural muscles in the hypodynamia model have been observed in other models of postural muscle inactivation. Restructuring in the myosin isoenzyme spectrum similar to that occurring under weightlessness was also observed after hypodynamia treatments of postural muscles.

The author argues that the essential factors in the situations described are gravitational unloading of the muscles and elimination of the tonic component of movement. In all probability, it is for precisely this reason that, when both fast- and slow-twitch muscles are subjected to inactivation, the latter show greater changes in speed characteristics. When the support function of the hindlimbs is eliminated, the soleus muscle is more sensitive than the extensor digitorum longus. When the distal portion of the forelimb is amputated, the postural muscle of the shoulder (medial head of the triceps) reacts analogously, while the mass and strength properties of the flexor brachial muscle show virtually no changes in the amputated leg.

A qualitatively different set of symptoms is observed in the postural muscles of animals subjected to a long period of restricted mobility: mild atrophy with a slight increase in relative mass of the muscles, decrease in amplitude of tetanus without changes in the ratio between A_T and muscle mass, and slower contraction and relaxation in tetanus.

When animals are maintained in cramped cages, i.e., under conditions that are commonly called hypokinesia, inactivation of postural muscles in rats evidently does not occur, especially during the first month of exposure. On the contrary, data attest to an increase in the motor activity of the animals during this time, accompanied by signs of pituitary-adrenal system activation and other manifestations of stress.

Slower contractions of isolated soleus and plantaris muscles, while absolute muscle strength remains the same (soleus), or increases (plantaris) after longer periods of hypokinesia (90, 120 days), can be considered a specific biomechanical effect of this model. These effects may be induced by

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increased loading on the extensors of the foot (when the animals are maintained in cramped cages, the ankle joint is usually flexed backward).

Because the effect of hypokinesia on postural muscles was unexpected, the author attempted to verify the results by artificially imposing tonic activation on the muscles by subjecting the animals to long-term exposure to acceleration (centrifugation). Isolated muscles and fibers were studied after exposure to acceleration of $+2G_x$, and $+1.03G_x$ (single fibers only).

Acceleration leads to a selective increase in the strength and work capacity of extensor muscle fibers performing an antigravity function (medial head of the triceps and soleus), attesting to the significantly greater functional loading on them than on the flexor muscles (extensor digitorum longus and brachial muscle).

Comparing results obtained from animals in the two experimental groups accelerated at $2-$ and $1.03G_x$ showed that seemingly functionally identical postural muscles -- soleus and medial head of the triceps -- reacted differently to the experimental conditions. The soleus muscle underwent changes only at an acceleration of $+2G_x$, while changes in the contractile properties of the medial head of the triceps were statistically significant and in the same direction in rats exposed to both accelerations. This may be explained by the morphofunctional and biomechanical characteristics of the medial head of the triceps. Although an active antigravity muscle, its speed of contraction makes it a fast-twitch muscle and, according to data obtained earlier, it contains predominantly FR fibers. The higher sensitivity to acceleration of the medial head of the triceps may result from its location in the forelimbs which in rats are comparatively more active in highly differentiated movements. This muscle also showed a unique pattern of changes after space flight. Changes in strength and work capacity were virtually identical in direction and magnitude to those occurring in the soleus muscle, while changes in speed of contraction were in the same direction as those in the brachial muscle -- the fast-twitch muscle of the forelimbs.

The author argues that the main reasons for adaptive changes in the postural muscles of rats in space flight are their unloading and a deficit in the tonic component of movement due to weightlessness. The reaction of the fast-twitch muscles under these conditions is mediated by behavioral adaptation and may be due to inclusion of these muscles in uncharacteristic, tonic activity.

Changes in Motor Unit Structure and Activity

The third group of experiments was directed at verifying that the new functional properties of muscles arising through adaptation to long-term changes in the biomechanical environment and may be maintained when no longer appropriate after previous conditions of motor activity are restored. In these experiments various manifestations of motor activity in animals were studied after exposure to various models entailing disuse of the motor system, using a device for in vivo recording of the mechanical properties of the contractions of individual muscles (dynamomyogram) in dogs.

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Biomechanical and kinematic characteristics of movements were also studied.

Hypokinesia in dogs was created using a system of restraints that prevented the animal from moving in space, but allowed it to "choose" one of three positions ("standing," "sitting," "lying") and enabled recording of spontaneous motor activity. A model of hypodynamia was created by encasing one hind limb in plaster with the knee at an angle of 150° and the ankle in a position of plantar flexion.

The dynamic characteristics of muscle contraction and movement were studied while the animals were performing a series of functional tests. Parameters recorded during the tests were used to compute parameters of muscle contraction in a single locomotive cycle in the muscles of the hind limbs (gastrocnemius, tibialis anterior, plantaris, and quadriceps).

The results of this research illustrate that, despite differences in the biomechanical characteristics of the models of muscle inactivation used on dogs, they all lead to some restructuring of the physiological characteristics of muscles, which show symptoms of functional insufficiency. This is accompanied by disorganization of movements manifested through: unstable gait, increased rate of locomotion, lengthening of the period of support; increased amplitude and rate of vertical displacements in the distal joint of the hind limbs; and disproportionate increase in the energy of bioelectric activity of muscles. It should be noted that analogous changes in kinematics and biomechanics of locomotion have been observed in humans after space flight and long-term bed rest. In accordance with the hypothesis under discussion, it might be assumed that the motor disturbances occurring after space flight result from different rates of recovery for the fast and slow muscles. In other words, on return from space, or, in analogous situations, operative control of movement returns to its previous mode but must act on muscles that still retain their newly acquired, in this case "space-adapted" functional profiles.

The results obtained reconfirm the fact that the contractile properties of the skeletal muscles are highly changeable or dynamic under conditions of weightlessness, as well as in other situations where the functional requirements on the muscles ("external input") alter substantially due to changes in the required movements.

It has been found that the contractile properties of skeletal muscles with different functions are transformed under experimental conditions, including space flight, in strict accordance with changes in the external mechanical requirements imposed. The author suggests that these restructurings involve motoneurons.

After 60 days of hypokinesia when reliable differences occur in various muscle groups of rats, electrophysiological testing of motoneurons established that the previous general increase in excitability of motoneurons of the spinal cord begins to be differentiated. Excitability decreases in the extensor pool, while features of stable hyperpolarization are retained in motoneurons of the flexor muscles. Under the same treatment and after approximately the same period of time, cytochemical studies revealed signs of atrophy in nerve cells in the spinal cord. Absolute and relative levels

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of RNA and proteins decreased. Analogous changes were observed in nerve cells of the spinal cord and cerebellum of rats flown on COSMOS biosatellites.

Turnover of water-soluble proteins in the motoneurons of the lumbar spinal cord also shifted, suggesting that functional activity was depressed. Immediately after reentry and during the readaptation period, clear signs of protein metabolism activation were observed in the motoneurons. Levels of proteins and RNA in the large neurons of the spinal cord ganglia also decreased.

The author believes that the immediate cause of such shifts may be restructuring of the nature and amount of afferent nerve activity. A direct consequence of such changes in the functional state and metabolism of motoneurons may be modified neurotrophic effects on the muscles. Alteration of the way information is transmitted from motoneuron to muscle may be significant. This conclusion is supported by the structural changes in nerve terminals and neuromuscular junctions observed in rats after space flight.

Thus, the neurotrophic factor may cause skeletal muscle reprogramming by initiating the synthesis of contractile and sarcoplasmic proteins. The constant degradation and renewal of these proteins creates an unstable equilibrium among the protein components of the muscle, which adjusts the myosins and other protein constituents in every muscle to fit environmental requirements. The rate of change of the neurotrophic system is limited by the turnover rate of contractile proteins. The turnover rate is different in the cardiac muscle and slow- and fast-twitch skeletal muscles. The turnover rate of various sarcoplasmic proteins can also vary within the same muscle fiber. This may be the source of the heterochronicity in changes in protein and enzyme complex metabolism in muscles, especially in response to various models of muscle inactivation. .

Unlike the neurotrophic control system, the fast response system of motor and postural control, adapts quickly. This system can itself be subdivided into systems of immediate ("operative") and slow ("conservative") adaptation to weightlessness. The first subsystem accounts for the almost instantaneous redistribution of postural muscle activity in weightlessness. The second is manifested toward the end of a 7-day space flight by loss of anticipatory activity in certain muscles that were previously critical to maintaining posture. The second type of postural adaptation is probably also dependent on neurotrophic processes, which are manifested at the neuromuscular as well as interneuronal (intracentral) levels.

It has not been ruled out that interaction of the operative and homeostatic regulation contours, for example when adapting to new conditions of motor activity, occurs in a continuum of regulatory subsystems (neuroreflexive, neurohormonal, neurotrophic), which differ from each other with respect to the time range required (from milliseconds to days and weeks) to establish the new equilibrium. However, there is overlap between the parameters of muscle structure or functions that these subsystems will regulate.

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Summary and Conclusions

In summary, the sensitivity of the skeletal muscles in mammals to changes in the magnitude of the gravitational field is a result of evolution. The reaction to weightlessness is systemic in nature, but its manifestations in different muscles depend on the extent to which each muscle participates in antigravity activity, its functional and metabolic profile, and the nature of the changes in specific biomechanical requirements.

The greatest sensitivity to weightlessness is noted in the antigravity muscles. Judging from the results of research, two types of adaptive reactions occur in these muscles in space flight: disuse atrophy and restructuring of the functional and metabolic profiles of certain fibers. It has been well established that both types of adaptive reactions are active processes and involve the nervous system.

In postural muscles, these adaptive changes are caused by the effects of weightlessness and are induced by a direct decrease in gravitational loading on the muscles and a deficit in the tonic component of movement. The functional manifestations of changes in the fast-twitch flexor muscles evidently result from behavioral adaptation of animals to the whole set of space-flight factors and are appropriate to the new conditions for movement. Adaptive changes in the postural and flexor muscles are reversible after flights lasting up to 22 days.

The described effects of space flight and simulation models on the skeletal muscles are mediated by neurotrophic factors which control the state of muscles. It is hypothesized that the slow-acting homeostatic contours that regulate the structural/functional organization of muscles "adjust" their profile according to the changing requirements of the external "mechanical field." This capacity is inherent in the dynamic organization of protein and energy metabolism of the muscles. Gravity-dependent changes observed in skeletal muscles are a special case of their functional flexibility.

Adaptive changes associated with the slow-acting control system are conservative in principle, as are its recovery mechanisms. For this reason, when there is a sudden drastic change, for example, from one level of gravity to another and back, adaptation of the skeletal muscles to each of these changes does not occur immediately.

There is reason to believe that adaptive changes in skeletal musculature developing in space flight (in the absence of prophylactic measures), may be one explanation for the motor disturbances occurring during the readaptation period. The recovery process could be marked by a lack of synchronism between neurotrophic remodeling of structural/functional characteristics and the operative requirements imposed by the environment.

MUSCULOSKELETAL SYSTEM

M137(20/88) Nasledov GA (editor).

Mekhanizmy neyronal'noy regulyatsii myshechnoy funktsii [**Mechanisms of neuronal regulation of muscle function.**]

Leningrad: Nauka; 1988.

[137 pages; 1 table; 21 figures; 501 references; 52 in English]

Affiliation [book]: Scientific Council on Problems of Biological Physics; I.M. Sechenov Institute of Evolutionary Physics, USSR Academy of Sciences

KEY WORDS: Musculoskeletal System, Skeletal Muscles, Fast- and Slow-Twitch, Motor Function, Neurophysiology, Neurological Control, Adaptation, Protein Turnover, Rats, Dogs, Humans, Space Flight, Short-Term, Soyuz-9, COSMOS-605, -690, -936, -1129, Immobilization, Hypokinesia, Hypodynamia, Tail-Suspension, Amputation, Motor Patterns

Annotation: This collection contains material presented at the second scientific conference on "Neural control of the structural and functional organization of muscles" (Repino, 1984), devoted to the problem of neurotrophic influences regulating the activity of physical-chemical and morphological characteristics of muscle units. Information concerning the mechanisms for which neurotrophic control of individual components of the neuromuscular system is presented and analyzed. Various effects of disrupted neurotrophic control on muscle functioning, including disease and weightlessness, are considered. Control of muscle proprioceptive receptors is discussed.

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NEUROPHYSIOLOGY

(See also: Biological Rhythms M142; Immunology M139;
Musculoskeletal System P944, M137)

PAPERS:

P914(20/88) Trinus KF.

Individual differences in variability of vestibular sensitivity as measured by subjective sensations and long-latency vestibular evoked potentials.

Fiziologiya Cheloveka.

14(4): 562-568; 1988.

[21 references; 9 in English]

Author's Affiliation: Kiev Scientific Research Institute of Industrial Hygiene and Occupational Disease

Neurophysiology, Vestibular Sensitivity, Evoked Potentials
Humans, Individual Differences
Acceleration, Threshold

Abstract: This work is devoted to a formal analysis of individual differences in subjective sensitivity thresholds and latent periods in the peaks of long-latency vestibular evoked potentials recorded under exposure to threshold acceleration. Sensitivity thresholds and latencies were recorded by unspecified methods in a total of 18 healthy individuals: sensitivity was studied in 12, evoked potentials in 17, and both functions in 11. Subjects were exposed to linear acceleration upward, the mean magnitude of which varied from 0 to 20 cm/sec². Each subject was tested repeatedly (on the same or different days) and a total of 120 trials were run. Statistical analysis was performed on the data.

Individual variations in the sensitivity thresholds were as follows: 1) threshold of nondiscriminating sensitivity, i.e., the acceleration for which a subject senses motion but cannot identify direction, (T1) ranged from 4.7 to 12.7 cm/sec², mean 8.3 cm/sec²; 2) threshold of inverted sensitivity, where sensed direction is opposite to actual direction of motion (T2), ranged from 6.3 to 16.9, mean 12.2 cm/sec²; 3) threshold of discriminated motion, where subject identifies direction correctly (T3) ranged from 7.7 to 22.4, mean 17.7 cm/sec². Individual coefficients of variation (error of the mean divided by mean) varied from 0 to 32% for T1, from 1.9 to 24.6% for T2, and from 0.5 to 20.9% for T3. Interindividual variation was 1.5, 0.8, and 1.9 times that of intraindividual variation, for T1, T2, and T3, respectively. Threshold of evoked potential for various individuals ranged from 3.8 to 7.6%. The mean coefficient of variation ranged from 0 to 39.5%. Ratio of inter- to intraindividual variability was 2.7. Relationships between magnitude of acceleration and latency of the three peaks (two positives and an intervening negative) characterizing an evoked potential were computed in each of the sensitivity threshold ranges.

The authors come to the following conclusions:

1. When the amplitude of a vestibular stimulus at threshold level increases, human subjects experience different sensations and thresholds of sensitivity, with progressive increase in the range of accelerations in which the sensory phenomenon and vestibular evoked potential occurs. The greatest stability (lowest ratio of intergroup variability to intragroup variability) occurs for the threshold at which reverse motion is

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experienced (T2) and the greatest individuality (highest value of above ratio) occurs for the threshold of accurate perception of motion direction (T3).

2. As acceleration increases in magnitude, the ratio between inter- and intraindividual differences in latent periods of evoked potential peaks decreases.

3. Individuals can be classified into groups on the basis of low, intermediate, or high variability in the latency of vestibular evoked potential peaks; those with intermediate variability are most numerous.

4. The latency periods of peaks of vestibular evoked potentials are higher in individuals who show higher variability in these latencies.

5. A group was identified which showed low values for the latency periods of vestibular evoked potential peaks. These subjects showed elevated variability in the negative peak of evoked potential; this peak normally shows least variability.

Table 1: Variability of latent periods of vestibular evoked potential peaks in subjects in different groups

Table 2: Changes in the structure of variability of latencies of vestibular evoked potential peaks as stimulus increases in various groups of subjects

Table 3: Changes in the structure of variability of latent periods of peaks in vestibular evoked potential as a function of magnitude of acceleration in various groups of subjects

Table 4: Distribution of groups of subjects, absolute values of peaks, individual and interindividual coefficients of variation as a function of level of acceleration

Table 5: Distribution of groups of subjects, absolute values of peaks, individual and interindividual coefficients of variation as a function of subjective sensation

P919(20/88)* Smirnov SA, Ayzikov GS, Kozlovskaya IB.

The effect of adaptive biofeedback control on the severity of vestibular and autonomic symptoms in experimentally induced motion sickness.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 35-39; 1988.

[14 references; 12 in English]

Neurophysiology, Motion Sickness, Induced
Humans
Psychology, Biofeedback

Abstract: It has been demonstrated that use of multichannel biofeedback (i.e, simultaneously providing information about a number of autonomic parameters) can be used to increase tolerance for situations inducing motion sickness in individuals (pilots) with relatively high levels of vestibular tolerance. The present experiment tested the effects of less cumbersome monochannel biofeedback (information provided only on skin temperature and conductivity) in individuals with low or average vestibular tolerance. Of the 27 subjects, 22 had average vestibular tolerance (mean tolerance for motion sickness inducing treatment 4-6 minutes) and 5 had low tolerance (mean tolerance time 2-3 minutes). [Motion sickness induction is called "standard" but not further described; evidently rotation.] Skin resistance and skin temperature were selected as biofeedback parameters because they change in a regular fashion as motion sickness symptoms develop. Before the experiment began all subjects participated in a total of 12 15 - 20 minute biofeedback training sessions, three sessions each were devoted to learning how to raise and lower each of the parameters. Subjects were selected for inclusion in the study who had mastered techniques for voluntarily regulating skin resistance by ± 5 kOhms and temperature by $\pm 5^\circ$ C. In the first condition, subjects were given a biofeedback session immediately before the beginning of rotation in which they spent 15 minutes attempting to affect one of the parameters. Subjects were instructed before rotation that they were to attempt to stabilize the parameter during the interrotation intervals and to raise it to baseline value using skills developed through biofeedback. The biofeedback signal was not available during rotation. In the second condition, no preliminary biofeedback sessions were given. The biofeedback signal was made available 5 minutes before rotation and remained on until the end of the experiment. Verbal instructions were identical to those in condition 1. An American-made biofeedback device (Autogen) was used in which changes in the pitch of a sound corresponded to changes in the level of the targeted parameter. Each condition included five rotation sessions. The first was devoted to determining initial vestibular-autonomic tolerance, and the fifth to determining level of adaptation to repeated exposures. Sessions 2 and 4 were used to evaluate effectiveness of use of biofeedback to decrease motion sickness. In session 3, subjects were asked to perform mental arithmetic as a control for the mental activity involved in the biofeedback procedure. To assess the importance of the individual difference variable, subjects with varying initial vestibular tolerance were compared after each subject participated in a single 5-trial cycle. To compare the two types of biofeedback, individuals with average tolerance participated in one cycle each of the two biofeedback conditions with the two sessions separated by 7 days. Four experiments were run. In experiment 1, biofeedback condition 1 was used on eight subjects with average tolerance); in experiments 2 and 3

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the second biofeedback condition was run on 9 and 5 individuals with average tolerance, respectively; in experiment 4 the biofeedback condition 2 was used on 5 subjects with low tolerance. Parameters recorded included skin resistance and temperature, respiration rate and inhalation amplitude, heart rate, galvanic skin response (GSR) and blood pressure.

When the first type of biofeedback was used, changes in tolerance of various rotation cycles depended on which parameter was being regulated. When skin temperature was regulated, no change in tolerance resulted. However, when the parameter was skin resistance, tolerance increased significantly. When the second biofeedback condition was used, tolerance increases were more pronounced. Subjects fell into two subgroups: in 3 subjects, regulation of skin temperature led to an increase of tolerance amounting to 90-150% of baseline value; in 5 subjects regulation of skin temperature had no effect on tolerance. When skin resistance was the regulated parameter both groups displayed marked increase in tolerance amounting to 50-150% of baseline. Use of the second biofeedback condition was significantly different for subjects with low and average initial tolerance. While use of biofeedback significantly increased tolerance in those with average tolerance, there was no significant effect on low tolerance subjects. Values of GSR appeared to be highly associated with the effects of biofeedback on tolerance. When tolerance increased, GSR was typically significantly lower than baseline during the rotation. Subjective rating of motion sickness symptoms also accorded well with actual increases in tolerance time.

Table: Effects of biofeedback on vestibular-autonomic tolerance

Figure 1: Effects of biofeedback condition 1 on vestibular-autonomic tolerance

Figure 2: Effects of biofeedback condition 2 on vestibular-autonomic tolerance

Figure 3: Comparative effect of the use of biofeedback condition 2 on rotation tolerance of subjects differing in initial vestibular-autonomic tolerance

Figure 4: Effects of biofeedback on severity of motion sickness symptoms in individuals with average vestibular-autonomic tolerance

P924(20/88)* Antipov VV, Tikhonchuk IB, Ushakov IB, Fedorov VP.

State of synapses of rat telencephalons under exposure to space flight factors.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 54-61; 1988.

[33 references; 3 in English]

Neurophysiology, Telencephalon, Synapses

Rats

Space Flight Factors, Radiobiology, Ionizing Radiation, Head, Acceleration, Vibration, Microwaves, Hypoxia, Hyperoxia

Abstract: The goal of this study was to evaluate the effects of exposure to single and combined space flight factors on synapses in various structures of the telencephalon. Structures examined include the sensorimotor cortex, caudate nucleus and hippocampus. These structures are associated with voluntary and reflexive motor acts and with memory and behavior in rats. Factors considered included hypoxia, hyperoxia, vibration, super high frequency fields, and ionizing radiation. Subjects were 280 Wistar rats exposed to a number of space flight factors either alone or in combination with gamma irradiation of the head in doses of 10, 50, and 200 Gy at a dose rate of 12 cGy/sec. Before, during, and after irradiation, the irradiation chamber was ventilated with ordinary air, a hypoxic gas medium (8% oxygen), or pure normobaric oxygen at a rate of 8 l/min. Duration of exposure to the altered atmosphere either separately or in combination with a radiation dose of 10 Gy was 6 min, with radiation dose of 50 Gy -- 18 minutes, or with radiation dose of 200 Gy - 55 minutes. Under all conditions, concentration of carbon dioxide never exceeded 0.3%. Before irradiation or immediately after, some subjects underwent +G_z acceleration of 5-G for 2.5 minutes, vibration at a rate of 8 m/sec² at the frequency of 80 Hz (to which the central nervous system is most sensitive), or to microwave irradiation (2.45 GHz) with power density of 300 mW/cm² for 20 seconds. The interval between exposures was 15 minutes. Animals exposed to a single factor were sacrificed 1.7 hours after exposure, while those exposed to a factor combined with irradiation were sacrificed 1.7 hours after the latter. Brain samples were fixed for electron microscopy by infiltration in a 2.5% solution of glutaraldehyde on a 0.2 M colloid buffer, facilitating rapid penetration of the brain. Additional fixation occurred in a 1% solution of osmic acid, then the tissue was dried in ethanol and the tissues samples from the sensorimotor cortex - field FPa and FPP; hippocampus - cellular layer of field A4; head of the caudate nucleus) and hardened in epoxy resin. Ultrathin sections were contrast stained and examined with an electron microscope. For each group of subjects, experimenters counted the total number of synapses on the dendritic thorns (the largest group of interneuronal contacts characterized by high reactivity and plasticity) in the sensorimotor cortex and determined the percentage of those which were unchanged or showed destructive or reactive changes. Status of the remaining interneuronal contacts was evaluated visually.

Irradiation of the head at 10 Gy had no significant effects on the structures studied. Irradiation of 50 Gy did not affect the majority of contacts in these structures, but some changes, swelling of presynaptic boutons and changes in numbers of vesicles, did occur. These are considered reversible changes. The highly labile structure of the axodendritic synapse of the cerebral cortex showed swelling, electron-dense

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inclusions, disorientation, and even disintegration. Membranes of postsynaptic structures proved highly resistant to this factor. However, synapses with destructive changes (especially, of the light type and focal degeneration) were common. When irradiation dose increased to 200 Gy a typical cerebral syndrome developed. The majority of changes in synapses could be classified as degeneration of the light type. The most labile were the synapses on dendritic thorns. In the sensorimotor cortex only 28% retained their normal ultrastructure. Short-term hyperoxia had no significant effect on the synaptic structure. Interaction between hyperoxia and radiation depended on dose of the latter and sequence of exposure to the two factors. When hyperoxic exposure occurred after radiation in a dose of 200 Gy, the changes were more severe and common than when either factor was applied alone. The most characteristic effect of this combination was rapid disintegration of structures with the formation of myelin figures and membrane complexes in presynaptic and postsynaptic elements. Short-term hypoxia alone did have a significant effect. Changes found were mainly functional, but degeneration of the light and (less often) focal type were encountered, especially in the sensorimotor cortex, when exposure was 55 minutes in duration. When radiation dose was 50 and 200 Gy and hypoxia preceded or was accompanied by irradiation, radiation effects were attenuated. Irradiation at 200 Gy followed by hypoxia enhanced radiation damage, especially in the sensorimotor cortex. Vibration lasting 1 hour at 800 Hz was associated with a number of apparent reactive changes: increased osmophilia of the pre- and postsynaptic elements plus an increase of osmophilic material in the synaptic cleft. Irradiation at 10 and 50 Gy preceded by vibration revealed no differences from irradiation alone. However, when vibration was combined with irradiation at 200 Gy or followed the lower doses, radiation effects were enhanced. Acceleration induced only reactive changes in the synapses of the brain structures. All vesicles, even in altered synapses, were more homogeneous in size, shape and osmophilia than after exposure to other factors. When acceleration preceded irradiation at 50 Gy [apparently the only level of irradiation combined with acceleration] a clear antagonistic effect was revealed (i.e, effects of irradiation alone were attenuated); when the temporal sequence of these factors was reversed, a synergistic effect was found. Microwave radiation alone did not induce significant changes in synapses. If electromagnetic irradiation preceded gamma irradiation (50 Gy only dose used), radiation effects were attenuated. If the factors were combined in the reverse order, radiation damage was intensified.

The authors conclude that the interneuronal contacts in the brain are highly sensitive to a number of flight factors, especially high doses of ionizing radiation and hypoxia. Synapses, on the other hand, are highly resistant to short-term hyperoxia and microwave radiation. When other flight factors are combined with ionizing radiation, changes in interneuronal contacts depended on dose of radiation and temporal order of exposure to the two factors.

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Table 1: Changes in axospine synapses in the sensorimotor cortex 1.7 hours after exposure to a factor (in %)

Factor	Synapse Changes		
	Unchanged	Reactive	Degenerative
Irradiation of the head:			
10 Gy	60.5	29.4	10.1
50 Gy	39.8	36.2	24.0
200 Gy	28.4	39.6	32.0
Hypoxia	51.2	32.1	16.7
Hyperoxia	62.5	26.6	10.9
Acceleration	58.9	26.5	14.6
Vibration	59.9	28.9	11.2
Electromagnetic fields	62.2	27.3	10.5
Control	79.2	15.4	5.4

Table 2: Nature of the interactions between certain space flight factors on the status of synaptic ultrastructures in the telencephalon of rats

Factor	Test-factors — irradiation of the head, Gy		
	10	50	200
Hypoxia			
before irradiation		-	-
during irradiation	none	-	-
after irradiation		none	+
Hyperoxia			
before irradiation		none	none
during irradiation	none	none	+
after irradiation		+	+
Vibration			
before irradiation	none	none	+
after irradiation	+	+	+
Acceleration			
before irradiation		-	
after irradiation		+	
Electromagnetic field			
before irradiation		-	
after irradiation		+	

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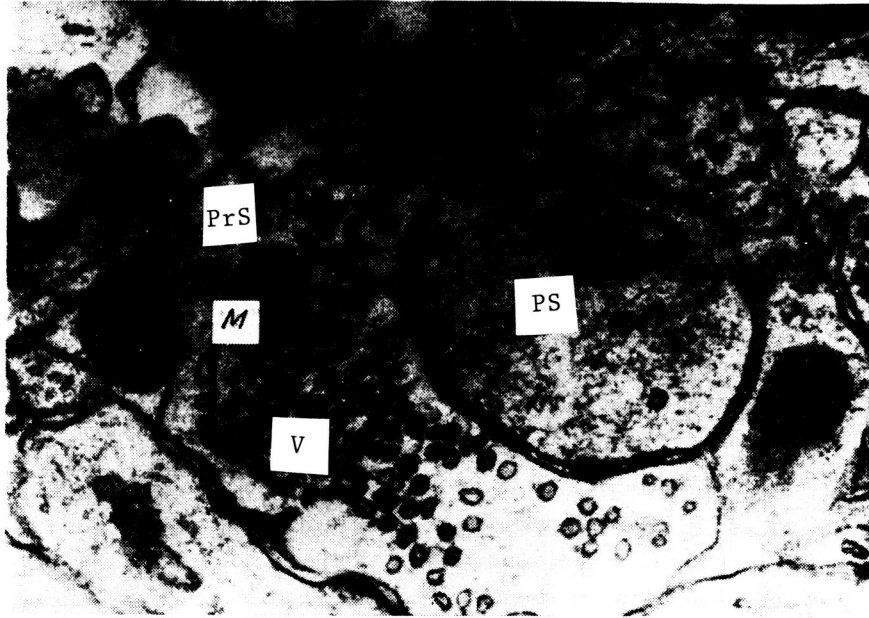


Figure 1: Sensorimotor cortex after irradiation in a dose of 10 Gy
Focal degeneration of the presynaptic elements of vesicles. Electronogram
X 80,00. Here and in Figures 2-4, PrS and PS are presynaptic and
postsynaptic elements; V - vesicle; M - mitochondria.

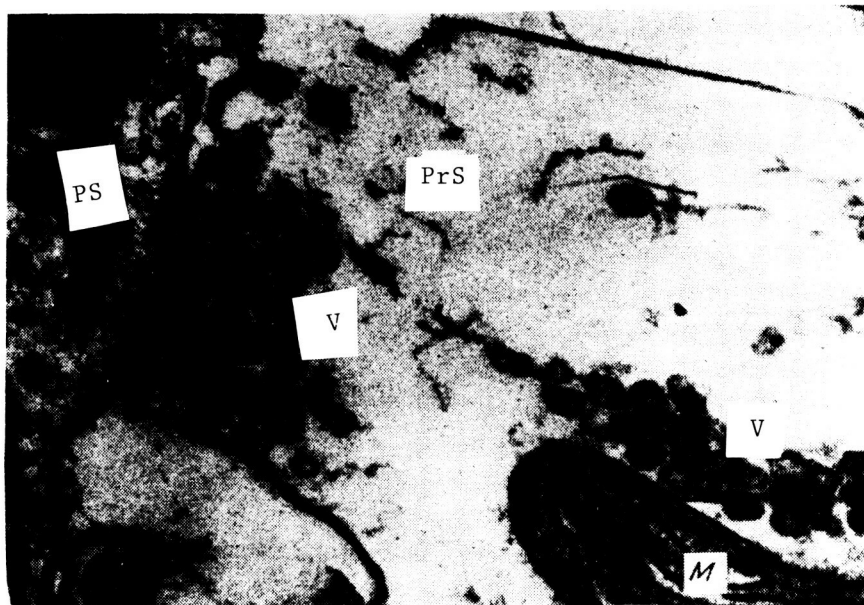


Figure 2: Sensorimotor cortex after irradiation at a dose of 50 Gy.
Swelling of the presynaptic elements, inhomogeneous degeneration of synaptic
vesicles, disintegration of presynaptic membrane. Electronogram X 100,000.

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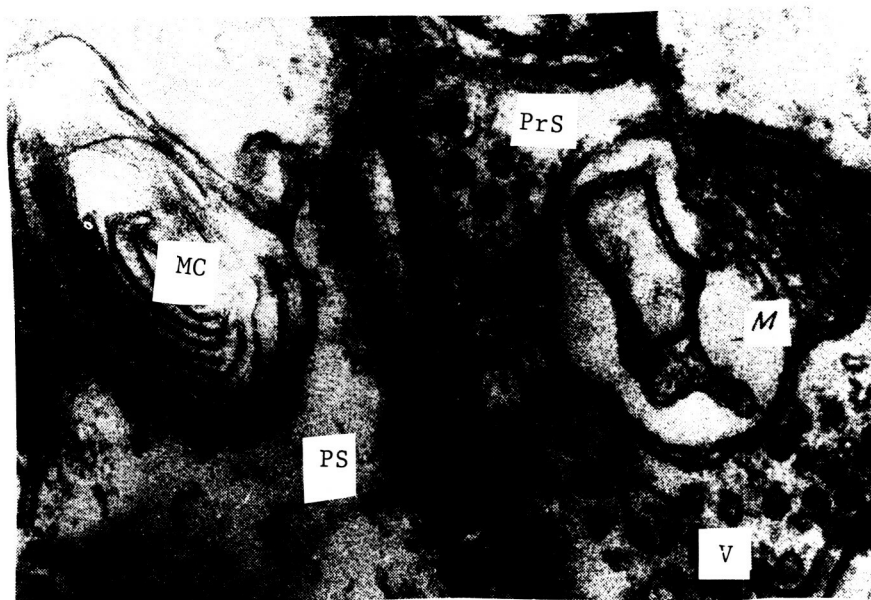


Figure 3: Sensorimotor cortex after irradiation in dose of 200 Gy under conditions of hyperoxia.

Membrane complex and postsynaptic region of degenerating synapse.
Electronogram X 94,000; MC - membrane complex.

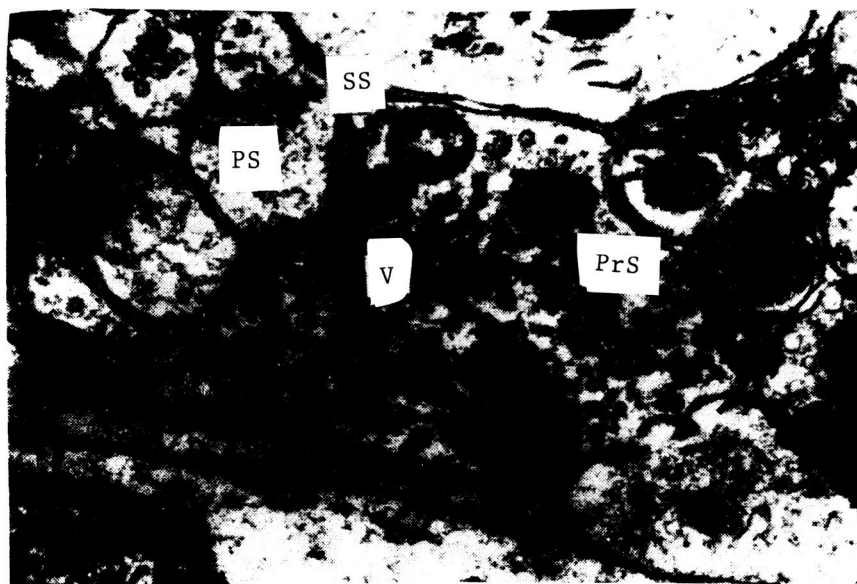


Figure 4: Sensorimotor cortex after exposure to vibration.

Synaptic cleft filled with osmophilic material. Electronogram X 64,000.
SS - synaptic cleft.

P933(20/88)* Galle RR, Gusakova GA, Sabayev VV, Galle NN.

Evaluation of the effectiveness of pharmacological countermeasures in preventing motion sickness.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 90-93; 1988.

[16 references; 9 in English]

Neurophysiology, Motion Sickness

Humans, Males

Pharmacological Countermeasures, Evaluation

Abstract: This paper presents a procedure, based on quantitative changes in clinical symptoms of motion sickness, which the authors developed for evaluating the effectiveness of drugs for preventing motion sickness. They summarize the results of using this procedure to test effectiveness of drugs against motion sickness induced by prolonged rotation. Subjects in the experiment were 26 apparently healthy men, aged 24-45, with heightened susceptibility to motion sickness. Subjects were rotated at 6 revolutions per minute for 5 hours. The following drugs and doses were studied: scopolamine (0.6 mg), phenkarol (quinuclidyl-3-diphenylcarbinol hydrochloride) (50 mg) + ephedrine (25 mg); phenkarol (50 mg) + sydnocarb (N-phenylcarbamoyl-3-(beta-phenylisopropyl)-sydonimine) (5 mg); pipolphen (promethazinehazine hydrochloride, an antihistamine blocking H_1 receptors) (25 mg) + ephedrine (25 mg), kavinton (ethyl ester of apotartaric acid, a vasodilator used to improve circulation in the brain) (10 mg); kavinton (10 mg) + scopolamine (5 mg). All drugs were taken orally in capsules 1 hour before rotation began, with the exception of kavinton which was taken 3 times a day for 7 days prior to rotation. The effects of the drugs were compared to those of a placebo using a double blind technique. Individuals rated the severity of motion sickness they were experiencing on a 5-point scale (excellent, good, satisfactory, poor, very poor). Based on differences between ratings before and after the drugs, effectiveness was rated on a 7 point scale (excellent, good, moderately positive, weakly positive, no effect, and negative effect). An individual's rating was called the individual coefficient of effectiveness. A drug was considered effective if an individuals coefficient was moderately positive or above, and ineffective otherwise. Two values were used to reflect the overall effectiveness of the drug: mean individual coefficient and percentage of subjects for whom the drug was effective.

Results of the study are presented in the table below. The authors point out that gastrointestinal symptoms of motion sickness should not be used as the sole criterion for the effectiveness of a drug as a countermeasure. Results based on increases in time elapsed before onset of vomiting led to a different rank ordering of drugs, with scopolamine being less effective than the placebo. The authors conclude that the use of their procedure leads to the most useful assessment of motion sickness drugs.

Table 1: Determination of individual coefficient of effectiveness

Table 2: Summary rating of the effectiveness of a drug

Figure: Histogram of latency of onset of pronounced motion sickness symptoms in subjects treated with pharmacological countermeasures or a placebo

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Table 3: Comparative effectiveness of motion sickness drugs

Parameter	Rotation without drug	Rotation with Drug						
		1 (n=26)	2 (n=26)	3 (n=9)	4 (n=5)	5 (n=5)	6 (n=11)	7 (n=1)
Frequency of symptom, %								
vomiting	50	30.4 (5)	11.4 (3)	0 (1)	20 (4)	40 (7)	36.4 (6)	10 (2)
nausea	100	78 (7)	50 (3)	44 (2)	60 (5-6)	60 (5-6)	55 (4)	20 (1)
sluggishness	65	48 (6)	38 (5)	60 (7)	20 (1)	25 (2)	32 (4)	28 (3)
headache	80	52 (4)	62 (6)	80 (7)	50 (3)	54 (5)	35 (2)	20 (1)
Mean rated severity of symptoms	11.0	9.5 (7)	6.8* (4)	6.8 (5)	6.7 (3)	9.1 (6)	5.8* (2)	5.4* (1)
Mean effectiveness coefficient	—	1.1 (6)	2.0 (5)	2.4* (4)	2.6* (3)	1.0 (7)	2.6* (2)	2.7* (1)
Effectiveness of drug, %	—	18 (7)	45 (5)	55 (4)	60 (3)	20 (6)	64 (2)	70 (1)
Sum of ranks	—	42	31	30	22.5	38.5	22	10
Overall rank	—	VII	V	IV	III	VI	II	I

Numbers in parentheses refer to rank ordering of drugs with respect to individual criteria; * -- differences between drug and placebo conditions significant with $p < 0.05$.

1- placebo; 2 - scopolamine (0.6 mg); 3 - pipolphen (promethazine hydrochloride, an antihistamine blocking H_1 receptors) (25 mg) + ephedrine (25 mg); 4 - phenkarol (quinuclodol-3-diphenylcarbinol hydrochloride) (50 mg) + ephedrine (25 mg); 5 - phenkarol (50 mg) + sydnocarb (N-phenylcarbamoyl-3-(beta-phenylisopropyl)-sydonimine) (5 mg); 6 - kavinton (ethyl ester of apotartaric acid, a vasodilator used to improve circulation in the brain) (10 mg); 7 - kavinton (10 mg) + scopolamine (5 mg)

P936 (20/88)* Lychakov DV.

Structural tolerance of vestibular receptors of exposure to space flight factors.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 13-19; 1988.

[40 references; 15 in English]

Neurophysiology, Vestibular Receptors, Damage Resistance
Fish, Amphibians, Larvae, Developmental Biology, Rats
Space Flight, COSMOS-782, -936, -1514, -1667

Abstract: The authors review the literature on the effects of space-flight factors on vestibular regulators. These effects can be divided into environmental conditions that act directly to stimulate the vestibular system (weightlessness, acceleration, vibration, noise, etc.) and those that act on other organs and tissues to indirectly affect the vestibular system (changes in ion exchange, hormonal changes, etc.). Results of laboratory experiments on vestibular effects of individual or paired space flight factors are presented in Tables 1, 2, and 3. It will be seen that these results may be quite contradictory.

Multiple studies involved exposure of developing larvae of fish (Fundulus heteroclitus and Brachydanio rerio and amphibians (Rano temporaria and Xenopus laevis) to space for 2 - 29 days. At launch larvae were at different stages of vestibular development. Larvae were either fixed on board or returned to earth and studied in the laboratory. Analysis techniques included: light, electron, polarizing, and scanning microscopy; X-ray microanalysis, chemical analysis and morphometry. All experiments showed that larvae of amphibians and fish developing in weightlessness show normal formation of the maculae, chrysta and otolith apparatus. However, the otolith membrane in the utricle of spurred frogs exposed to weightlessness for 8-9 days was 1.3 times the size of that of a control group. Although full studies of the response of vestibular structures in adult fish and amphibians to space flight have not been performed, the authors did study the otoliths of 2 adult female guppies, which had been housed in an airtight container on COSMOS-1514 for 5 days. No significant changes in otolith weight or asymmetry were noted. Examination of cross sections of the saccular otoliths revealed damage to the outermost growth layer, but this may have occurred during slide preparation.

The effects of weightlessness on the vestibular systems of rats were studied in animals flown on COSMOS-782 and -1514. Unfortunately, flight rats suffered from bleeding in the inner ear or otitis after landing, which may have confounded the results. This did not occur with subjects on COSMOS-936 or -1667. The utriculi and sacculi of rats were studied with a light and electron microscope, after animals had completed a 20-day (COSMOS-936) or 7-day (COSMOS-1667) flight. No major pathological changes in the structure or ultrastructure of the vestibular system were noted, nor were there any large differences in the crystal structure or ultrastructures. At the same time, small structural changes in the ultrastructure of the nuclei of receptor cells were noted in COSMOS-936 rats, while there was increased swelling of the chalice-shaped nerve endings after flight on COSMOS-1667.

The general conclusion from these and U.S. flight studies is that no major changes occur in the structural organization of the vestibular system in the

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animals studied which can be attributed to space flights of up to 20 days. However, the possibility of adaptive restructuring in this system cannot be ruled out. To definitively decide the issue of adaptive changes in the otolith, long-term studies must be performed. The best subjects for such studies are fish which have an otolith apparatus that is not a collection of small statoconia, but a single large otolith. This otolith may be weighed and analyzed for chemical components and its growth rings measured. Due to structural heterogeneity of the receptor organs of the vestibular system, when comparisons are made of flight and control animals, it is essential to know exactly from which region the studied cross sections were taken. Existing knowledge of the fine structure of the neural nets in the receptor epithelium is inadequate to this enterprise and must be improved to enable further study of space flight effects.

Tables 1: Effects of acceleration on the receptor organs of the vestibular system

Animal	Acceleration, g	Duration, min.	Nature of Structural Changes
Guinea pig	10	3	LM - RNA nucleolus outside of the nucleus in receptor cells TEM - small ultrastructural changes in receptor cells
Guinea pig, rabbit	10	5	LM, TEM - marked changes in all receptor cells of the maculae and in the otolith membrane
Squirrel monkey	5.49 10.92	10 1	LM, TEM - no changes in the maculae " " " " " " "
Squirrel monkey	12-25	3.25-5.5	LM - start of loss of statoconia from otolith membrane, but no changes in maculae
Guinea pig	200-400	Peak	LM - in some macula areas, destruction of supporting and receptor cells
Squirrel monkey	60 200 450	1 1 Peak	LM - start of loss of otoconia from otolith membrane LM, TEM - no changes in maculae TEM - increased size and changes in the structure of the lysosome in receptor cells and transformation of mitochondria in the chalice-shaped nerve endings

Here and in Tables 2 and 3: LM = light microscopy; TEM = transmitting electron microscopy.

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Table 2: Effects of vibration and noise on the receptor organs of the vestibular system

Animal	Treatment	Frequency	Intensity	Duration	Structural Changes
Guinea pig	Vibration	6-8 Hz	Accel. vib. 1-2 g	6 hours	LM - in some maculae, change or loss of part of the statoconia, destruction of some receptor and supporting cells
Guinea pig	Noise	Wide band	154 dB	20 min.	LM - compression and rupture of otolith membrane
Rat, mouse	Noise + vibration	Vib.: 50 Hz mid freq noise	Accel.vib. 9 g, noise 100 dB	3 hrs/day for 1 yr	LM - degenerative changes in neuro-epithelium of ampulla and maculla of the sacculus only after many months
Guinea pig	Noise	Geometric mean, 2000 Hz	100 dB	Single & multiple exposure over 7 days	TEM - noticeable ultra-structural changes in receptor cells, nerve fibers, and capillaries

Table 3: Effects of factors related to changes in ion exchange and redistribution of body fluids on the receptor organs of the vestibular system

Animal	Treatment	Duration, days	Structural Changes
Macaque	Horizontal hypokinesia, then hypokinesia with head-down tilt	7 12	TEM - no changes in vestibular or auditory organs of the labyrinth
Macaque	Sitting position, then hypokinesia with head-down tilt	2 7	As Above.

Table 4: Otolith weight (in ug) in guppies flown of COSMOS-1514

Conditions	Fish #	Otolith of left labyrinth			Otolith of right labyrinth		
		utric.	saccul.	lagena	utric.	saccul.	lagena
Control	1	28	246	35	21	228	28
"	2	27	210	34	8	200	32
Flight	3	33	227	38	9	228	32
"	4	16	215	31	10	220	28

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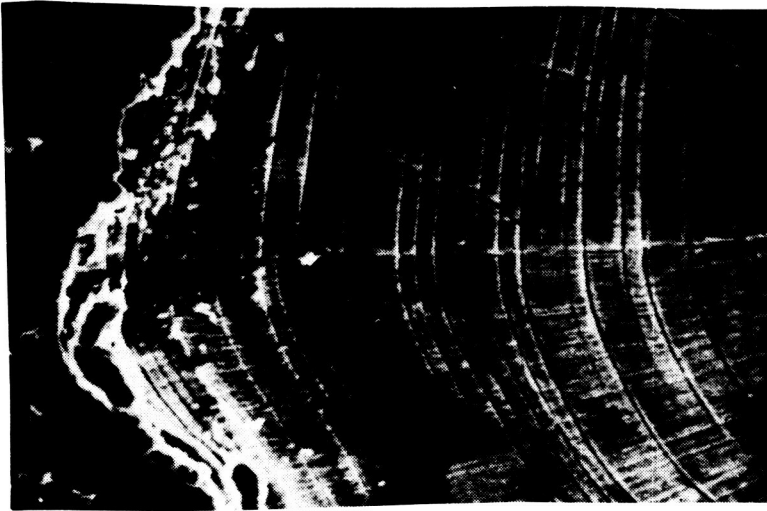


Figure: Portion of a cross section of the saccular otolith of a guppy.
Growth layers clearly visible. Outermost layer (on the left) damaged.
Scale: 50 μ m.

P939(20/88) Belichenko PV.

Quantitative analysis of dendritic thorns of pyramidal neurons in layer V of the sensorimotor cortex of rats flown on COSMOS-1667.

Byulleten' Eksperimental'noy Biologii i Meditsiny.

CV(6); 736-738; 1988.

[11 references; 5 in English]

Author's affiliation: Brain Research Institute, USSR Academy of Medicine.

Neurophysiology, Sensorimotor Cortex, Neurons, Dendritic Thorns

Rats

COSMOS-1667

Abstract: The density of dendritic thorns in the pyramidal neurons of layer V of the sensorimotor cortex was studied in rats exposed to space for 7 days on board COSMOS-1667. Four groups of 3 male Wistar rats served as subjects: the flight group, a vivarium control for the flight group, a ground-based synchronous control group exposed to all space flight factors except weightlessness, and a vivarium control for the synchronous group. The frontal portion of the sensorimotor cortex was removed 3 minutes after sacrifice and impregnated using Golgi's silver technique. Thorns were counted in pyramidal neurons in a 100 μ m of layer V of the sensorimotor cortex under a microscope with magnification 312 X. This number was computed separately for the right and left hemisphere for apical and branched dendrites passing through layers III-IV, for apical dendrites passing through layers I-II, and for basal dendrites. No data were collected on layers I-II of the left hemisphere. For each subject, the number of dendritic thorns was counted for 5 neurons, so that there were 15 parameter values for each group. Statistical significance was tested against the Kolmogorov-Smirnov criterion, and results were expressed as a median.

Results are presented in the table below. No differences were found between the right and left hemisphere or in the number of thorns on basal and apical dendrites passing into layers I-II. The most pronounced changes occurred in layers III-IV, in which the number of apical dendrite thorns increased reliably in the flight and synchronous conditions (by a mean of 21% compared to control). A 26% increase occurred in the flight group for branched dendrites compared to all other groups. In other environmental experiments, increases in dendritic thorns have been associated with positive, rather than negative, environmental factors (e.g., increased exercise, enrichment of the environment).

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Table: Number of thorns in large pyramidal neurons in a 100 μ m area of layer V of the sensorimotor cortex in rats (median value)

Dendrites	Hemi- sphere	Group			
		Flight	Viv-1	Sync.	Viv-2
Basal	R	41	47	43	33
	L	44	33	39	42
Apical: layers III-IV	R	61*	55	58*	47
	L	55*	40	51*	45
Branched: layers III-IV	R	54**	44	46	46
	L	58**	42	45	46
layers I-II	R	18	16	16	14
	L	--	--	--	--

* difference between flight or synchronous group and corresponding vivarium control significant, with $\alpha = 0.05$; ** difference between flight and other three groups significant with $\alpha = 0.95$.

P940(20/88) Pozdnyakov OM, Babakova LL, Demorzhi MS, Il'ina-Kakuyeva YeI.
Changes in the ultrastructure of motoneuron synapses in rats exposed to space flight factors.

Byulleten' Eksperimental'noy Biologii i Meditsiny.

CV(6); 752-755; 1988.

[5 references; 2 in English]

Authors' affiliation: Institute of General Pathology and Pathological Physiology, USSR Academy of Medicine; Institute of Biomedical Problems, USSR Ministry of Health.

Neurophysiology, Musculoskeletal System, Motoneuron Synapses, Ultrastructure
Rats
Space Flight, COSMOS-1667

Abstract: This experiment investigated the ultrastructure of neuromuscular synapses in striated muscles differing in their functions in rats exposed to a 7-day space flight on COSMOS-1667. Portions of muscles were taken from the synaptic zones of the soleus, gastrocnemius and diaphragm muscles of 6 Wistar SPF rats flown on COSMOS-1667 and 7 analogous rats in a vivarium control group. The animals were sacrificed 4-8 hours after reentry. Tissue was fixed in 4% formaldehyde buffered to pH 7.4 with an acetate-veronal buffer plus isosmotic saccharose, then washed in a cold buffer. Postfixation occurred for 2 hours in a chilled 1% solution of OSO_4 , after which the sample was poured into araldite. Ultrathin sections were cut and contrast stained in a 15% solution of uranylacetate in methyl alcohol for 5 minutes and then reduced by tin citrate for 5-10 minutes.

The major change found in the soleus muscle of the flight animals was a decrease in synaptic contact area due to partial degeneration of presynaptic structures (axon terminals). One could see exposed areas of postsynaptic membranes, which were in contact with outgrowths of Schwann cells and the fibrous elements of connective tissue. Around such areas there were shafts of electron-dense basal membrane indicative of degeneration. Axons buds surrounded by Schwann cells were also observed. Individual motoneuron synapse terminals also exhibited lightening of the axoplasm and partial or even complete degeneration. The postsynaptic membranes formed many deep, sometimes anastomotic junctional folds with a clearly delineated cholinoreceptive zone. Junctional folds remained even when the axons terminals were completely destroyed.

In the neuromuscular synapses of the gastrocnemius muscles of flight rats the motor terminal layers extended along the muscle fiber and contained 5-6 small axon terminals with axoplasm of medium density. Throughout the free area of the terminals were many rounded, closely packed synaptic vesicles. The mitochondria were few in number. The junctional folds in the majority of synapses were short and of uneven width. The material in the cleft and folds was diffusely distributed. There was no clear cholinoreceptive zone. There were also degenerative changes in the terminal axons: areas of exposed postsynaptic membranes. In place of the terminal there were outgrowths of Schwann cells, vacuoles, bundles of parallel shafts of basal membrane substance. In places there was new growth of axons, i.e. signs of regeneration as well as destruction.

In the diaphragm, the majority of synapses had normal structures. No

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structural changes were noted in the cleft and folds. At the same time, some terminals showed partial lightening of the axoplasm and disorganization of junctional folds at the base of the neuromuscular connections.

The authors summarize these changes as follow: in the soleus there is an increase in degenerative changes in axon terminals that reflect unloading this muscle during weightlessness. At the same time, hypertrophy of the subneural apparatus, as seen in the increase in number of junctional folds, may be due to an adaptive response to the decreased secretion of the synaptic transmitter. In the gastrocnemius, changes seem to involve as altered organization of axon terminals and presynaptic areas, accompanied by a decrease in synaptic contact area. These changes can be related to decreased muscle use in space. Changes in the diaphragm may be a morphological reflection of increased function after reentry. The authors describe all changes as functional and likely to be reversible.

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Figure: Neuromuscular synapses of rats after a 7-day space flight
a-neuromuscular synapse of the soleus muscle: shrinking of the area of synaptic contact due to axon terminal degeneration (mag. 23,000); b - neuromuscular synapse of the gastrocnemius muscle: axon terminals contain many synaptic vesicles; synaptic folds somewhat deformed, shortened and broadened, and electron density of their substance is uneven (mag. 37,000); c - neuromuscular synapse of diaphragm muscle: presynaptic and subsynaptic areas did not differ from normal (mag. 20,000)

Key: AT- axon terminal; SC- synaptic cleft; JV - junctional fold; N - nucleus; OSC - outgrowths of Schwann cells; SV- synaptic vesicles ; M- membrane; MF membrane fragment

P942(20/88) Drozd YuV, Yasnetsov VV, Shashkov VS.

On the vestibuloprotective characteristics of certain regulatory peptides.

Byulleten' Eksperimental'noy Biologii i Meditsiny.

CVI(7): 50-52.

[15 references; 7 in English]

Authors' Affiliation: Institute of Biomedical Problems, USSR Ministry of Health

Neurophysiology, Vestibular System, Motion Sickness

Cats

Pharmacological Countermeasures, Enzymology, Regulatory Peptides

Abstract: A number of regulatory peptides have been shown to prevent chemically-induced emetic response in cats. This experiment tested the capacity of these peptides to prevent or ameliorate motion sickness in animals. Subjects were 12 male cats, which 3-5 days prior to the experimental treatment had had a cannula implanted in the cavity of ventricle IV of the brain. Regulatory peptides in doses of 10-100 ug were dissolved in sterile physiological saline solution 50-100 ul, injected 1-3 minutes before motion sickness induction. Motion sickness was induced by vertical and horizontal acceleration during a 1-hour period. Severity of motion sickness was rated. The following regulatory peptides were used: alpha, gamma and des-Tyr¹-gamma endorphin, undecapeptide hydra, swine beta-lipotropin, ACTH₁₋₃₉, and substance P. Naloxon (L-17-Allyl-4,5-epoxy-3,14-dihydro-morphinan-6-on), a universal blocker, was used to block the opioid receptors, as well as the selective delta-blocker ICI 154,129. Scopolamine was also tested.

Four of the regulatory peptides, gamma and des-Tyr¹-gamma endorphin, substance P, undecapeptide hydra, had effects comparable to those of scopolamine injected systemically, as did naloxon. The other regulatory peptides (Beta-lipoprotein, ACTH, and alpha endorphin), as well as intraventricularly administered scopolamine, did not prevent the development of motion sickness in cats. The effectiveness of naloxon injected intraventricularly suggests that central opioid mechanisms play an important role in the development of motion sickness. The fact that ICI 154,129 has some ameliorating effect on the symptoms suggests the various types of opioid receptors participate. The lack of positive effect of beta-lipotropin and ACTH can be explained by the fact that regulatory proteins do not have an antiemetic effect with regard to morphine and beta-endorphin. However, gamma and des-Tyr¹-gamma endorphins, substance P, and undecapeptide hydra prevent vomiting induced by opioids, and this explains their positive prophylactic effects. The efficacy of a whole series of endorphins of the alpha type in preventing motion sickness in cats suggests that other central peptidergic mechanisms, aside from endogenous opioid peptides, play a role in pathogenesis of motion sickness.

Table: Prophylactic effects of regulatory peptides and blockers of opioid receptors compared with scopolamine in induced motion sickness in cats

NUTRITION: See Body Fluids CR11; LSS P907

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(See also: Cardiovascular and Respiratory Systems M140)

PAPERS:

P910(20/88) Chadov VI, Iseyev LR, Polyakov VN.

The hypobaric normoxic cabin atmosphere and minimum acceptable level of working pressures in an EVA space suit.

In: Malinin VB, Kosmolinskiy FP, Kuznets YeI (editors).

Perspektivy Razvitiya Kosmicheskoy Biomeditsiny v Svete Idey K.E.

Tsiolkovskiyogo [Prospects for the Development of Space Biomedicine in Light of the Ideas of K.E. Tsiolkovskiy] Proceedings of the XXth and XXIst Lecture Series dedicated to the scientific legacy and development of the ideas of K.E. Tsiolkovskiy., Kaluga 1985, 1988. Section on Problems of Space Medicine and Biology.

Moscow: USSR Academy of Sciences: 1987.

Pages 113-123.

[24 references; 3 in English]

Operational Medicine, Human Performance, EVAs

Humans, Cosmonauts

Habitability and Environment Effects, Cabin Atmosphere, Space Suit Pressure

Today, development of the principles for creating a hypobaric atmosphere in hermetically sealed cabins of spacecraft and scientific justification for the values of the major parameters of such an atmosphere are important concerns of researchers working on the problem of supporting decompression safety of space flights. Interest in this technique for preventing high-altitude decompression disorders can be attributed to the fact that such atmospheres would make it possible to use lower levels of working pressure in space suits, while at the same time retaining or even increasing decompression safety. This would lead to a significant advance and improvement in the mobility of the space suit, and thus increase the work capacity of the person wearing it.

The most extensive research in this area was performed by a group of scientists led by P. M. Gramenitskiy. The authors studied the effects of long-term (up to 24-48 hours) exposure to an artificial nitrogen-oxygen environment, containing 40 or 45% oxygen with an overall pressure of 0.551 atm. (540 gPa), on the likelihood of high altitude decompression disorder arising in humans after decompression and 6 hours of work under conditions of residual pressure of 0.23 atm. (226 gPa). The major result of this work was the finding that high altitude decompression disorders were relatively frequent in subjects exposed to the atmosphere with 40% oxygen and were virtually nonexistent with 45% oxygen. Based on these results, one can conclude that during EVA from a spacecraft with an artificial atmosphere with total pressure of 0.551 atm., a space suit with working pressure of 0.23 atm. may be used only if there is no less than 45% oxygen in the cabin atmosphere. However, considerations of fire safety (exceeding the maximum acceptable level of 40% oxygen concentration in a hermetically sealed environment) cast doubt on the possibility of actually utilizing these conditions. The minimum level of working pressure that could be recommended

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for an EVA space suit with a hypobaric normoxic cabin atmosphere containing no more than 40% oxygen, unfortunately, has not been determined.

For this reason, the authors attempted to identify the minimum acceptable working pressure for a space suit and the major parameters of the cabin atmosphere (pressure, oxygen and nitrogen content) which, under conditions of no less than 24 hours of preliminary exposure, would ensure decompression safety on transition to that space suit pressure. This was the goal of the present study.

Research was performed in a barochamber 110 m³ in volume. Two experiments were performed. Each consisted of two preliminary and one major stage. The first preliminary stage simulated possible conditions in a spacecraft cabin immediately before launch and, in both experiments, involved 2 hours of exposure to an atmosphere with total pressure of 1.142 atm. (1120 gPA). The second preliminary stage lasted 24 hours and simulated living conditions of cosmonauts during the first day of orbital flight in a spacecraft cabin with lowered total pressure and normalized partial oxygen pressure. Conditions of normoxic hypobaria were created by decreasing pressure in the chamber and simultaneously increasing oxygen concentration. Values of these parameters were as follows: pressure 0.580 atm. (569 gPA), oxygen concentration 38%; pressure 0.620 atm. (608 gPA) oxygen concentration 36%, in the first and second experiments, respectively. The volunteers did not perform any special physical work during the preliminary stages of the experiments. The main stage of the experiment simulated work conditions during EVA in space suits with working pressure of 0.24 atm. (experiment 1) or 0.25 atm. (experiment 2). During this stage, the subjects breathed a gas mixture consisting of 95% oxygen and 5% nitrogen. The face portion of a gas mask was used to deliver oxygen. Duration of the main stage was 6 hours. During this time the volunteers performed periodic graded physical exercise with their arms, involving moving a special two-shoulder lever, located at chest level, back and forth at different rates. Total duration of the work and rest periods in each hour was 40 and 20 minutes, respectively. Energy expenditure varied between 4 to 6 calories/minute, depending on work rate. High altitude decompression disorder was diagnosed on the basis of the subjects' reported symptoms and objectively noted clinical symptoms. A total of 32 volunteers, males aged 21 to 47, participated in this study. Experimental conditions and results are presented in the table below.

As the table shows, the first experiment involved a total of 35 trials using 25 subjects. A total of 24 subjects (9 participating twice) fully completed the research program. During the final stages of the experiment, they responded adequately to their surroundings, accurately and rapidly performing all the instructions of the experimenter. In no case did a subject complain of anything suggesting deterioration of general state or well-being.

A single subject, who participated in the experiment twice, displayed signs of high-altitude decompression disorder in both instances. In the first case, during the second hour of the final stage, he developed diffuse reddening of the skin on the anterior surface of the chest cavity to the left, which by the end of hour 4 had developed in the form of a hyperemic

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spots of a petechial eruption 4X6 cm in size which itched a great deal. He was transferred to the lock compartment and "brought down to Earth." The itching stopped at 0.397 atm (389 gPa), but the hyperemic spots did not disappear "on Earth" and were still present in the clinic after several hours. After 6 months, in the next experiment, this same subject began to develop unpleasant symptoms 1.5 hours after the beginning of the final stage of the experiment, followed by increasing pain in the right knee joint. He again was brought down and the joint pain ceased at a pressure of 0.448 atm. (440 gPa). These symptoms were interpreted as the muscle-joint form of high altitude decompression disorder of degree II.

The fact that some subjects systematically developed clear, although differing, symptoms of high altitude decompression disorder under the decompression conditions studied, led to attempts to find other schedules that would more reliably ensure decompression safety. Evidently, safety during transition to a residual pressure of 0.24 atm. could have been increased through supplemental decrease of the partial pressure of nitrogen in the initial atmosphere by means of additional decrease in the overall pressure and increase of oxygen to 40%. However, this schedule was not tested experimentally, since positive results thus obtained could not be implemented in practice due to the fact that 40% concentration of oxygen in the atmosphere of a cabin would have had to be recommended as the lower boundary of regulated pressure. This would have meant that the settings of equipment responsible for maintaining the necessary concentration of oxygen in the cabin atmosphere would have nominal values exceeding the maximum acceptable 40% level for fire safety. Increasing the magnitude of residual pressure (working pressure in the space suit) while maintaining baseline conditions also did not appear desirable, since when residual pressure increased, there might be some increase in the overall pressure of the initial atmosphere and a decrease, in accordance with requirements of normoxic, of the concentration of oxygen, which would have some effect on the purely technical problem of creating and maintaining the artificial hypobaric atmosphere in the hermetically sealed environment.

For these reasons, a second experiment was performed to study the probability of development of high altitude decompression disorders in humans performing physical work under conditions of residual pressure of 0.25 atm. after preliminary exposure to an artificial nitrogen-oxygen medium with 36% concentration of oxygen and overall pressure of 0.62 atm. The major result of this experiment (31 trials) was the absence of any incidence of high altitude decompression disorder in any of the 26 subjects, including the one who developed symptoms in both trials of the first experiment. These results demonstrate that a hypobaric normoxic gas medium with overall pressure of 0.62 atm., containing 36% oxygen and 64% nitrogen, is an artificial atmosphere to which a subject can be exposed for not less than 24 hours to effectively prevent occurrence of high altitude decompression disorder during the next 6 hours of moderate physical exercise at a residual pressure of 0.25 atm. The latter pressure of 0.25 can be considered the practical attainable minimal value of working pressure for an EVA space suit, which during an EVA from a spacecraft with a hypobaric atmosphere ($P_{\text{tot}}=0.62$ atm., $O_2=36\%$) ensures decompression safety for EVA and does not require additional desaturation (pure oxygen breathing) before locking.

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Exp.	Experimental Conditions			Table			
	Stage 1	Stage 2	Stage 3	# trials	# subjects	# cases of HADD	# subjs. with HADD
1	1.142 atm. 2 hours	0.58 atm. O ₂ =38% N ₂ =62% 24 hours	0.24 atm. O ₂ =95% N ₂ =5% 6 hours	35	25	2	1
2	" "	0.62 atm. O ₂ =36% N ₂ =64% "	0.25 atm. " " "	31	26	0	0

HADD = High altitude decompression disorders

P911(20/88) Malkin VB, Landukhova NE, Shishov AA.

A rapid method for training hypoxia [tolerance].

In: Malinin VB, Kosmolinskiy FP, Kuznets YeI (editors).

Perspektivy Razvitiya Kosmicheskoy Biomeditsiny v Svete Iday K.E.

Tsiolkovskiyogo [Prospects for the Development of Space Biomedicine in Light of the Ideas of K.E. Tsiolkovskiy] Proceedings of the XXth and XXIst Lecture Series dedicated to the scientific legacy and development of the ideas of K.E. Tsiolkovskiy., Kaluga 1985, 1988. Section on Problems of Space Medicine and Biology.

Moscow: USSR Academy of Sciences: 1987.

Pages 38-43.

[7 references; none in English]

Operational Medicine, Hypoxia Tolerance

Humans

Adaptation, Training Method

Research directed at increasing human tolerance of acute and chronic hypoxia has been performed for many years. It is well known that barochamber training is the most accessible and effective method for increasing human tolerance of high altitudes. Results of studies have demonstrated that after repeated ascents in a barochamber many subjects display marked increases in tolerance of oxygen deprivation, even if preliminary ascents are of short duration.

It is notable that all these works deal with training directed at increasing the "altitude ceiling." The possible use of barochamber training to increase tolerance of chronic hypoxia has not been but widely studied. Experience shows that the correlation between tolerance of acute hypoxia (stepwise ascents in the barochamber) and of chronic hypoxia (long-term stays in the mountains) is not high.

The present experiment was intended to study the effectiveness of barochamber training in increasing human tolerance of acute and chronic hypoxia. Every day for 3 days subjects were raised to an altitude of 6200 m in a barochamber in a series of 3 steps. On the first day, subjects were raised to a height of 4200 m, where they remained for 30 minutes (step 1); to 5200 m, where they stayed for 30 minutes (step 2); and finally to an altitude of 6200 m, where they stayed for 10-15 minutes. On the second day, the above training cycle was repeated, except that the duration of the stay at 6200 m increased to 15-20 minutes. On the third and final day, subjects remained at 6200 m for 25-30 minutes.

During training, electrocardiograms, electroencephalograms, and pneumograms were recorded and blood pressure was measured. To gain information about work capacity and evaluate emotional state, the subjects (10 young healthy males) were given various psychophysiological tests: multiplication of columns of two-digit numbers, work on the "Fiziolog" device; estimates of time intervals of 15, 40, and 60 seconds; and performance of moderate physical exercise.

The effectiveness of the training schedule was assessed by determining tolerance for acute hypoxia (stepwise ascents in the barochamber to an altitude equivalent of 9000 m) during long-term (up to 3 days) exposure of the subjects to an "altitude" of 4200 m in the barochamber and to the same

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altitude in the mountains (Caucasus, Shelter-11). Thus, effectiveness of the barochamber training was studied for both chronic and acute high-altitude hypoxia.

When barochamber training was conducted, all subjects tolerated exposure to the first step (altitude of 4200 m) well (due to the relatively low level of hypoxia induced). Differences in how they felt, and improvements after the second and third exposure occurred only at altitudes of 5200 m and particularly at 6200 m. On the day after training was complete, individual high altitude tolerance was determined by means of stepwise ascents in the barochamber.

Of 10 subjects for whom an "altitude ceiling" had previously been determined, the barochamber training schedule led to a marked increase in high altitude tolerance both during exposure to an altitude and during ascents in 7 subjects. In 2 subjects, tolerance time at a "height" increased only insignificantly and in 1 subject no effect was found.

In subjects who displayed improved high altitude tolerance, there was also a marked increase in work capacity at altitudes of 6000-8000 m. This capacity was indexed by performance of psychophysiological tests, including stereotyped conditioned reflexes, subjective estimation of short time intervals, solution of elementary arithmetic problems, and also the structure of their handwriting. It should be noted that of the 7 subjects displaying improved tolerance of hypoxia, only 1, during a period of impaired physiological state at the highest altitude, on his own initiative donned the oxygen mask (in accordance with preliminary instructions), while the others used the oxygen only at the request of the experimenter. Thus, subjects were not experiencing the sensation of oxygen deficit.

To evaluate the effectiveness of barochamber training on response to chronic hypoxia, research was performed with 9 young men. In this study, the subjects were raised in a barochamber to an "altitude" of 4200 m, where they remained for up to 3 days. Each subject participated in two high-altitude ascents: one before and one after barochamber training.

In a control condition untrained subjects experienced symptoms typical of altitude sickness (headache, dizziness, nausea, loss of appetite, insomnia) at varying intervals of time (from 4 to 20 hours) after ascent to a height of 4200 m. It is significant that the nature and severity of symptoms of altitude sickness during time spent at "high altitude" differed in different subjects, i.e., there were marked individual differences in tolerance of hypoxia. At the same time, correlations between an individual's tolerance of acute and chronic hypoxia were not high. In 3 of the 9 subjects, symptoms of acute high altitude sickness (headache, vomiting) were so severe in the control ascents, that the trial had to be terminated early during the first day of exposure to a height of 4200 m. In 4 subjects symptoms of high altitude sickness were moderately severe, and in 2 they were virtually absent, with a mild decrease in appetite being the sole indicator.

After high altitude training in the barochamber, all subjects spent a stipulated amount of time at 4200 m. Subjects showing the most serious

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symptoms of altitude sickness during control ascents displayed significantly less severe symptoms after training. After training, the remaining subjects felt well at a height of 4200 m, with virtually no symptoms of acute altitude sickness evident.

Thus, it was established that short-term high altitude training in a barochamber moderates the course of high altitude sickness and facilitates more rapid development of adaptation to chronic hypoxia.

When this barochamber training schedule was tested under actual high altitude conditions in the Caucasus (Shelter 11, 4200 m), positive results were also obtained.

P930(20/88)* Portnov FG, Slutskiyy LI, Vorob'yeva LF, Iyerusalimskiy AP, Vandan YaA, Sinel'shchikova MP.

Reactions of dermal connective tissue to exposure to an electrostatic field in rats.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 81-84; 1988.

[15 references; 1 in English]

Operational Medicine, Connective Tissue

Rats

Radiobiology, Electrostatic Field

Abstract: This paper presents the results of a study of the connective tissue components of skin to exposure to an electromagnetic field with voltage of 60 and 90 kV/m. Subjects, male Wistar rats, were irradiated in a condenser-type chamber, while control animals were housed in a similar chamber without irradiation. In one experiment, the field had voltage of 60 kV/m and in the second voltage was 90 kV/m. In both experiments, rats were placed in the chambers for 4 hours daily for 3, 14, or 30 days. There were 5 animals in each group. Material studied was the dermal connective tissue on the back. Quantitative biochemical analysis and semiquantitative histochemical methods were used to measure mucopolysaccharides and nucleic acids. Data were analyzed using analysis of variance.

After exposure to a field of voltage of 60 kV/m, only small marginally significant changes were noted in biochemical parameters and these only in the early and middle durations (increased hexuronic and sialic acids). After 3 days of exposure to the higher intensity field, concentration of DNA and hexoamines had decreased reliably. No significant changes were noted after 14 days of exposure, while after 30 days hexuronic acids and hexoses were elevated. In neither experiment did protein composition of the skin change. Thus glycoconjugates were more sensitive and informative indicators. The authors conclude that the biologic effects of electrostatic fields of 60 and 90 kV/m on the skin involve biochemical alterations of the connective tissue. However, adaptation occurs relatively rapidly at the lower voltage. At the higher voltage, early transient biochemical changes, suggesting inhibition of biosynthesis of glycoconjugates, give way to changes in the opposite direction in the concentration of carbohydrate-containing biopolymers.

Table 1: Biochemical parameters of the skin of rats after exposure to an electrostatic field with voltage of 60 kV/m

Table 2: Biochemical parameters of the skin of rats after exposure to an electrostatic field with voltage of 90 kV/m

P931(20/88)* Domashuk Yu. (Poland)

Tolerance of $+G_z$ acceleration by pilots with health problems.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 84-86; 1988.

[9 references; 4 in English]

Operational Medicine, Aviation Medicine, Acceleration Tolerance
Humans, Pilots, Patients
Population Study

Abstract: In this study, pilots of fighter aircraft who were certified for flight but identified as having some health problems were tested for their tolerance of $+G_z$ acceleration. Tolerance was identified as the units of acceleration at which the field of peripheral vision began to narrow. A total of 33.1% of the pilots tested were found to have some health problem. In order of diminishing frequency, these were: imperfect vision, degenerative changes in the spine, hearing deficit, stomach or intestinal ulceration, circulatory problems, renal colic, high blood pressure, psychological disturbances, neurosis, past traumatic injuries. Most of these pilots did not show tolerance different from that of pilots judged without health problems. Pilots with high blood pressure showed greater than normal tolerance for acceleration. Pilots identified as suffering from psychological disturbance and neuroses showed diminished tolerance.

Table: Tolerance of $+G_z$ acceleration in pilots with health problems

PERCEPTION

PAPER:

P918(20/88) Ivanov VV, Vorob'yev OA, Shipkov YuYu.

The development of spatial orientation in the process of flight training.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 31-34; 1988.

[21 references; 4 in English]

Perception, Spatial Orientation

Humans, Pilots

Pilot Training

Abstract: The authors argue that one of the most productive lines of study in the important area of human spatial orientation relates to the development and maintenance of the representation of spatial position during complex flight conditions. However, they believe that too much emphasis has been placed by researchers on the role in this representation of visual information (from the instrument panel) and too little on the sensorimotor component. They take the position that perception is action-based and that in the motion-orientation pair, motion takes precedence over orientation. Spatial orientation is considered a process. Appropriate orientation in space develops in student pilots as they begin to consider their spatial position as "merged" with that of the aircraft. This merged representation moves with respect to an invariant coordinate system mapped with respect to the Earth. Earlier, their own orientation is perceived in relation to the spatial coordinates of the aircraft cabin. The new orientation develops from the old through mastery of piloting control movements.

Thus, as flight experience increases, the pilot shifts to a geocentric spatial orientation system resulting from mastery of a new technique of moving through space (via aircraft control instrument). The new way of perceiving spatial perception in flight is linked with a mastery of a motor task new to the student -- that of moving (in an aircraft) along a complex trajectory in three-dimensional space. The conceptual structure of this task, realized in a schema for performing the piloting operations, becomes the key factor for developing a new perceptual system in which information is gathered and integrated both from the flight instruments and from other more familiar sources.

PERSONNEL SELECTION

PAPER:

P909(20/88) Voronin LI, Zhernavkov AF, Kalinichenko VV, Kravchenko VV, Ulyatovskiy NV.

On the development of K.E. Tsiolkovskiy's ideas in the area of predicting human gravitational tolerance during space flight.

In: Malinin VB, Kosmolinskiy FP, Kuznets YeI (editors).

Perspektivy Razvitiya Kosmicheskoy Biomeditsiny v Svete Idey K.E.

Tsiolkovskiyogo [Prospects for the Development of Space Biomedicine in Light of the Ideas of K.E. Tsiolkovskiy] Proceedings of the XXth and XXIst Lecture Series dedicated to the scientific legacy and development of the ideas of K.E. Tsiolkovskiy., Kaluga 1985, 1988. Section on Problems of Space Medicine and Biology.

Moscow: USSR Academy of Sciences: 1987.

Pages 12-16.

[4 references; none in English]

Personnel Selection

Humans, Cosmonauts

Orthostatic Tolerance

The possibility of a contingency landing by a spacecraft crew in an uninhabited area makes it necessary to select individuals for space flight who are able to retain orthostatic tolerance at the level required for performing acts critical to survival. This goal led to a search for the most reliable methods for predicting gravitational tolerance. To solve this problem, the authors used a provocative test involving acceleration that reproduces, in a more extreme form, the hemodynamic changes occurring in the space flight cycle. The essence of the proposed test is sequential exposure of the subjects to chest-back acceleration of up to 2.5-G at an angle of 90° (phase of accelerated hemodynamic simulation of weightlessness) and head-torso acceleration of up to 2.5-G at an angle of 5° (phase simulating early readaptation period).

When a subject showed good tolerance for this test, the decrease in orthostatic tolerance shown after 30 days of hypokinesia was minimal and when a subject showed poor tolerance, there was a marked orthostatic intolerance effect subsequent to hypokinesia.

In order to reveal propensity to show significant decreases in gravitational tolerance after space flight, a cosmonaut must undergo exposure to chest-back acceleration of 2.5-G for 1 hour and then 10 minutes of head-torso acceleration at the same magnitude. It proved desirable to search for a way to achieve the same prognostic power with a less grueling method.

Bearing in mind that excess pressure in the lower body (LBPP), inducing redistribution of blood in the cranial direction is significantly easier to tolerate than chest-back acceleration, the authors compared individuals' tolerance of a tilt-test with LBPP in a horizontal position followed by negative pressure on the lower body (LBNP) in a vertical position with results of the centrifugation test described above. This work was based on the assumption that the proposed test with chest-head followed by head-torso

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acceleration is predictive of orthostatic intolerance in a postflight period.

For the comparison, 11 apparently healthy subjects aged 20-37 were subjected first to an acceleration of $+2.5 G_x$ at an angle of 90° for 60 minutes followed by $+2.5 G_x$ acceleration at an angle of 5° for 10 minutes. Evaluation of tolerance for this tests used a binary rating system:

- diminished tolerance - the research had to be discontinued before completion for medical reasons;
- good tolerance -- the subject was able to complete the program without medical cause to terminate the test.

Next, after an interval of no less than 3 days, the same subjects were exposed to LBPP of 25 mm Hg in a horizontal position for 40 minutes, followed by LBNP of 25 mm Hg in upright position (at an angle of 70° to the horizontal) for 10 minutes.

The schedules of LBPP and LBNP for the orthostatic test were selected a priori, to be equivalent to the acceleration tests. In particular, LBPP at 25 mm Hg in a horizontal position was selected because when the hemodynamic factors of weightlessness are simulated by $+2.5 G_x$, true systolic pressure in the arteries of the legs decreased by 20-30 mm Hg in comparison to baseline.

To evaluate circulation in the head and tolerance for the given tests, on alternate minutes of exposure to LBNP in an upright position an impedance plethysmogram of the head was recorded using bitemporal leads and the "Levka-ZT" portable plethysmograph the dicrotic index was determined. Tolerance of the given test was evaluated using a binary rating system:

- diminished tolerance - the test was discontinued before completion due to development of orthostatic collapse or the dicrotic index decreased to 5% or below in response to LBNP in an upright position (precollapse state);

- good tolerance - the subject was completely able to tolerate the test for the stipulated exposure period or the dicrotic index as an indicator of vascular tonus in the head did not decrease below 10% during LBNP.

Results of the investigation were processed using nonparametric statistical criteria.

The results obtained from the comparative studied are presented in the table, which shows that the LBPP test in the horizontal position and LBNP in the vertical, in comparison to the test using $+2.5 G_x$ followed by $+2.5 G_z$, is a less stressful provocative test, since the latter had to be terminated before completion nearly twice as frequently.

The table gives the assessment of tolerance of the test in two variants: with or without simultaneous consideration of the value of the dicrotic index. When the results were analyzed statistically, the correlation between tolerance of the acceleration test and the altered lower body

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pressure test without consideration of dirotic index was not significant ($p > 0.1$). This correlation increased to 0.61 with $p < 0.05$ when the value of the dirotic index was taken into consideration.

Thus, when evaluation criteria included the value of the dirotic index, assessment of individual tolerance of the test with altered pressure showed good agreement with tolerance of the acceleration test.

On the basis of these results, the authors conclude that, by analogy with the sequential effects of $+G_x$ acceleration as a model of weightlessness and $+G_z$ acceleration as a model of orthostatic loading in the early adaptation period, sequential exposure to LBPP in the horizontal and LBNP in the vertical position are a promising test for predicting gravitational tolerance in the early readaptation period.

The results of this research also show that the severity of provocative tests may, in principle, be diminished without substantial loss of predictive validity due to improvement of methodological techniques for simulating hemodynamic situations arising in the course of a space flight, and of the physiological criteria used to assess endurance of particular factors.

Table: Comparative evaluation of tolerance of sequential exposure to $+2.5 G_x$ at an angle of 90° for 60 minutes and $+2.5 G_z$ at an angle of 5° for 10 minutes and tilt test in the horizontal with LBPP and LBNP in the vertical position

Subject	Tolerance of $+2.5 G_x$, $+2.5 G_z$ acceleration	Tolerance of tilt test with LBPP/LBNP ignoring DI	Dynamics of DI in upright position with LBNP					Tolerance of tilt test with LBPP/LBNP in- cluding DI
			2'	4'	6'	8'	10'	
1	good	good	50	38	25	65	35	good
2	good	good	82	86	70	65	83	good
3	good	good	62	50	70	40	32	good
4	good	good	35	0	0	15	5	diminished
5	diminished	good	20	33	20	5	5	diminished
6	diminished	diminished	60	0	0	5	5	diminished
7	diminished	diminished	33	4*				diminished
8	diminished	diminished	20	0	15	7*		diminished
9	diminished	diminished	15	40	10	8*		diminished
10	diminished	diminished	37	23	5	**		diminished
11	diminished	good	50	30	40	20	35	good

4*, 7*, *8* - minute during which the experiment was terminated due to pre-collapse symptoms

DI - dirotic index

PSYCHOLOGY: See Neurophysiology P919, Radiobiology P929

RADIOBIOLOGY

(See also: Neurophysiology P924; Operational Medicine P930.)

PAPER:

P929(20/88)* Malakhovskiy VN, Bobyr' BA, Bokk MM, Mikhaylichenko PP, Sergeyev AA.

Some physiological characteristics of the initial reaction to radiation and its apomorphine model.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

22(4): 77-81; 1988.

[25 references; 8 in English]

Human Performance; Psychology, Animal Learning

Dogs, Humans

Radiobiology, Early Response, Apomorphine

Abstract: Experiments were performed on 52 outbred male dogs weighing 15-20 kg. Some subjects were irradiated (type of radiation not specified) in doses of 5-80 Gy with dose rate of 0.02-0.05 Gy/min. Other subjects were injected subcutaneously with apomorphine in doses of 0.02-0.5 mg/kg. Clinical symptoms and behavioral changes were noted. Blood pressure was measured at the base of the tail. Maximal muscular force was measured by force exerted against a tensometric platform. To evaluate goal-directed behavior, a specially designed methodology involving sequentially overcoming obstacles of increasing difficulty was used. Obstacles were of two types: barriers of increasing height (30 to 210 cm) and beams of decreasing width. The former was considered to involve mainly physical effort, while the latter was more related to sensorimotor coordination. The most difficult obstacle overcome was recorded. Stimulus for task performance was the experimenter's command. Task motivation was considered to be high. Ten trials were run in a 30-minute period. The effect of apomorphine was also studied on 18 healthy men, aged 26-43. Subcutaneous dosage was 0.6, 1.2, or 3.4 mg per person. Four types of dependent variables were considered: 1) general state of well-being (interview, self-rating, activity level, mood); 2) active mnemonic performance and attention in memorizing 10 words, reaction time (simple and discriminative), tracking errors, and performance of disjunctive tests; 3) autonomic functions (pulse, electrocardiogram, pneumogram, blood pressure in horizontal and upright positions, body temperature); 4) electroencephalographic parameters. Data were considered significant when they differed from baseline values by more than 3 standard deviations.

During the first few hours after irradiation animals showed the classical early symptoms of radiation sickness; initial arousal followed by lethargy and gastrointestinal symptoms. After apomorphine injections, starting at a dose of 0.3 mg/kg animals showed initial arousal followed by weakness and lethargy. Stereotyped movements began to appear at a dose of 0.2 mg/kg and was present in all animals at doses above 0.3 mg/kg. Emetic responses occurred 5-30 minutes after administration of apomorphine and 1-3 hours after irradiation. In both groups, blood pressure dropped during this response and muscle force and sensorimotor coordination decreased after its

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completion. With respect to the emetic effect, a dose of 0.02-0.1 mg/kg apomorphine corresponded to irradiation dose of 6-8 Gy. For the other effects a dose of 0.02 mg/kg apomorphine was close to irradiation of 5 Gy, and 0.2 mg/kg of the drug was equivalent to irradiation of 10 Gy. Apomorphine effects persisted for 0.5-1.5 hours, while those of irradiation lasted 3-4 hours.

In humans, considerable individual differences were found in response to apomorphine. Dose at which 50% of subjects vomited was approximately 0.2 mg/kg. Much individual variability was seen in other dependent variables. Most subjects experienced sleepiness, listlessness, headache, other pain, salivation, occasional double vision, impairment of short-term memory, increase in sensorimotor reaction time, and tracking errors. Exercise tolerance decreased. On the basis of the data for the dogs, the authors postulate that changes found in humans at doses of 0.6-2.4 mg apomorphine will correspond qualitatively and quantitatively to early reactions to irradiation in doses of 5-10 Gy, but that radiation effects will last considerably longer. On the basis of data in the literature, the authors suggest that the common factor leading to the similarity in the effects of the two treatments is changes in dopaminergic systems in the brain. They conclude that the apomorphine model is promising for use in studying not only vomiting, but also other symptoms of initial reaction to radiation in humans.

Table 1: Emetic reaction of dogs to irradiation and injection of apomorphine

Table 2: Frequency and duration of significant ($\geq 3\sigma$) changes in parameters of functional state of subjects after injection with apomorphine

Parameter	Frequency, %	Duration, hours
Self-rating	83	1.2
Autonomic reactions	44	2.7
Cognitive work capacity	67	2.4
Electrocorticogram	65	2.6

Figure 1: Overcoming barriers by dogs in the initial hours following irradiation or injection with apomorphine

Figure 2: Walking on beams by dogs in the initial hours following irradiation or injection with apomorphine

Figure 3: Push? strength in dogs in the initial hours following irradiation or injection with apomorphine

Figure 4: Systolic blood pressure in dogs in the initial hours following irradiation or injection with apomorphine

MONOGRAPH:

M138(20/88) Moldotashev B.

Deystviye vysokogor'ya i ioniziruyushchey radiatsii na organizm zhivotnykh i fiziologicheskiye mexhanizmy povyshennoy radiostoychivosti [**The effects of high altitudes and ionizing radiation on animals and physiological mechanisms underlying heightened radioresistance.**]

Frunze: Ilim; 1987.

[155 pages; 239 references]

Affiliation [book]: Institute of Biochemistry and Physiology, Kirghiz Academy of Sciences

KEY WORDS: Radiobiology, Ionizing Radiation, Radioresistance; Adaptation, High Altitudes, Hematology, Hemopoiesis, Immunology

Annotation: This monograph presents the general laws underlying adaptive restructuring of the body at high altitudes and, particularly, the course of radiation sickness under these conditions. It has been found that high altitudes are associated with increased rate of proliferative activity of hemopoietic stem cells and lymphoid tissues, and also optimization of the immune system, fostering rapid elimination of the consequences of radiation damage. This book is intended for a broad range of physiologists, hematologists, immunologists, radiobiologists, oncologists, and physicians.

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REPRODUCTIVE BIOLOGY

(See also: Endocrinology P928)

PAPERS:

P937(20/88) Serova LV, Tikhonova GP, Denisova LA, Pustynnikova AM, Ivanov YuV, Baykova OV.

The state of spermatogenesis and reproductive function in rats after space flight on the COSMOS-1667 biosatellite.

Paper delivered at the XIXth conference of the Permanent Working Group of Socialist Nations on Space Biology and Medicine within the Intercosmos Program, Havana, 5-12 April 1986.

Authors' Affiliation: Institute of Biomedical Problems, USSR Ministry of Health, Moscow.

Reproductive Biology, Spermatogenesis, Reproductive Function

Rats, Male

Space Flight, COSMOS-1667

Abstract: Male rats (number not specified in abstract but believed to be 7 from other articles) were flown for 7 days on board COSMOS-1667. Postflight examination did not reveal differences in weight of the testes or epididymi, concentration of spermatozoid, or percentage ratios of various types of cells (germinative, Sertoli, Leydig, leukocytes) in homogenates of the testes. Flight rats were allowed to breed with normal females during a 15-day postflight period. Sexual activity of flight males was normal, and percentage of females becoming pregnant was actually higher when bred with the experimental group than with the controls. No significant differences in numbers of living or dead neonates, sex ratios in litters, birth weights, or anomalous offspring were found in litters fathered by flight and control rats.

P938(20/88) Denisova IA, Snetkova YeV.

The effects of short-term space flights on the reproductive function in animals.

Abstract of paper delivered to the XXIth Conferences of the Permanent working Group of Socialist Countries on Space Biology and Medicine, Intercosmos, 6-10 June. Baranov Sandomersky, Poland.

Authors' Affiliation: Institute of Biomedical Problems, USSR Ministry of Health, Moscow.

Reproductive Biology, Reproductive Function

Rats, Male

Space Flight, COSMOS-1887

Abstract: An unspecified number of male rats were flown for 2 weeks on COSMOS-1887. Postflight, the weight of the testes of flight animals was 12% below that of control, while the weight of the epididymus was 11% below that of a synchronous group. When weights of the reproductive organs were computed as a fraction of body weight, no differences between flight and control animals were noted. Nor were significant differences found in number of spermatogones, spermatocytes, spermatids, spermatozoids, Sertoli cells, or Leydig's cell in the tests or spermatozoids in the epididymi of flight and control animals.

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16. Abstract This is the twentieth issue of NASA's USSR Space Life Sciences Digest. It contains abstracts of 43 papers published in Russian language periodicals or presented at conferences and of 6 new Soviet monographs. Selected abstracts are illustrated with figures and tables from the original. A report on a conference on calcium metabolism is presented. The abstracts in this issue have been identified as relevant to 28 areas of space biology and medicine. These areas are: adaptation, biological rhythms, body fluids, botany, cardiovascular and respiratory systems, developmental biology, endocrinology, enzymology, equipment and instrumentation, exobiology, gastrointestinal system, genetics, habitability and environmental effects, hematology, human performance, immunology, life support systems, mathematical modeling, metabolism, musculoskeletal system, neurophysiology, nutrition, operational medicine, perception, personnel selection, psychology, radiobiology, and reproductive system.					
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